USE OF FUNCTIONALIZED ONIUM SALTS AS A SOLUBLE SUPPORT FOR ORGANIC SYNTHESIS

A subject of the present invention is the use of functionalized onium salts as a soluble support for organic synthesis.

Since the introduction of Merrifield's method for peptide synthesis (Merrifield, 1963), resin-type insoluble supports have been introduced into many syntheses in order to facilitate the purification of products and more particularly in the field of combinatorial chemistry during the last 10 years (Thompson et al., 1996; Toy et al., 2000; P.; Seeberger et al., 2000; V.,Krchn¡a'k and M., W. Holladay, 2002; Mütter et al., 1979; Han et al., 1995; Harris et al., 1992; Nicolaou et al., 2002; Kates et al., 2000). Although very effective, solid-support synthesis still suffers from a certain number of problems linked to the heterogeneous nature of the reaction conditions. In fact, the non-linear kinetic behaviour, the unequal distributions, the sites which are non-accessible to reagents, the problems of solvation, of pure synthesis posed by the solid phase as well as the complex identification of the grafted resins remain major handicaps for this methodology.

The drawbacks of solid supports have led to the exploration of alternatives in order to find homogeneous reaction conditions. In fact, the use of soluble polymers bypasses the difficulties of synthesis on solid supports whilst retaining a large number of its positive features. The term "Synthesis on soluble polymer or SPOS" is used for reactions in homogeneous liquid phase carried out on a soluble functional polymer which serves as a protective group and the macromolecular properties of which facilitate the purification of the products (Haag, 2001; Haag et al., 2002; Kim et al., 2000; Kim et al., 1996; Hovestad et al., 2000; Hodge, 1997; Frank et al., 1975; Han et al., 1997).

These liquid-phase methodologies avoid the difficulties of solid-phase synthesis, for example the non-linear kinetic behaviour, the distribution (unequal access to the interaction sites), the problems of solvation linked to the nature of the support, and the operating conditions which cannot be simply transposed between the standard organic reactions in solution and the solid phase. However, by replacing the insoluble crosslinked resins with soluble polymer supports, the advantages of the solid support are retained: standard reaction conditions in homogeneous medium but also easy

purification of the products. Moreover, the soluble supports present the possibility of analysis by the standard means used in organic chemistry such as UV-visible, IRTF and NMR spectroscopies as well as high-resolution mass spectrometry. Moreover, thin layer chromatography can be used to monitor the reactions without requiring preliminary cleavage of the support (Mütter et al., 1979; Han et al., 1995; Harris, 1992), which is an advantage of this technology. A rapid and effective characterization of the support is an important tool, particularly for parallel, combinatorial or multi-stage syntheses.

In the same manner as in solid phase, the soluble supports can be separated from the molecules of low molecular weight after each stage by ultrafiltration, dialysis, preparative exclusion chromatography (SEC), or precipitation. Even if the automation of these techniques is not as advanced as with resins, significant progress has been made in the last few years. The polymers which can be used as soluble supports must be commercially available or easily prepared, be chemically stable, be correctly functionalized in order to be able to attach an organic part and be very soluble in the usual solvents. In general the polymers are a mixture of molecules of different sizes which have different properties. The soluble supports should have a polydispersity as close to 1 as possible and a high enough molecular mass to be crystallized at ambient temperature. Most of the soluble polymers used have hydrocarbon skeletons (Janda polymers) or alkyl polyethers and more particularly polyethylene glycols (PEGs).

Up to now, the polymer most used as a soluble support in organic synthesis is monomethylated polyethylene glycol (MPEG 5000) containing only one OH or diol function and therefore has a low specific charge (0.2 mmol OH/g)(Mutter et al., 1974; Mutter et al., 1975; Gravert et al., 1997; Toy et al., 2000). More recently, PEGs with a higher specific charge have been prepared, being able to be purified by precipitation. These star-shaped (Chang et al., 1999; Knischka et al., 2000; Reed et al., 2000) or branched (Benaglia et al., 1998; Annunziata et al., 2000) PEGs at the terminal positions can reach specific charges of 1 mmol of OH/g of polymer but take a long time to prepare.

The linear polymers relating to the functional groups on each monomer unit, such as polyvinyl alcohol (Elias, 1997), the polyacrylamides (Wellings et al., 1987; Ranucci et al., 1994) and the polymers prepared by ROMP ("ring opening metathesis polymerization") (Barrett et al., 1999; Barrett et al., 2000; Barrett et al., 2000) have also been used in SPOS. These polymers with a high specific charge are problematical to use in certain cases because of their limited solubility and stability (Meier et al., 2001).

Also, perfect dendrimers (polyamidoamine, polysilane, polyester) have been used as supports in combinatorial synthesis. These polymeric soluble supports with a high theoretical specific charge are fragile, with relatively low molecular weights and are prepared by multi-stage route, which limits their use in combinatorial chemistry (Burgath et al., 2000).

The aliphatic dendritic polyethers (branched analogues of PEGs) are on the other hand chemically stable under many reaction conditions and should therefore be useful as polymer supports in organic synthesis. Moreover, the chemical properties of these materials are ideal for synthesis supported in solution. Moreover, the globular form of these dendritic polymers can promote their purification by membrane techniques (dialysis and ultrafiltration). The dendrimeric aliphatic polyethers containing 1-3 diol and 1-2 diol units have recently been prepared in 6-7 stages. They have specific charges of 6-7 mmol of OH/g but they take a long time to prepare and have relatively low molecular weights (Jayaraman et al., 1998; Grayson et al., 1999; Haag et al., 2000).

Haag recently reported the controlled synthesis of dendritic polyglycerols. These aliphatic polyol polyethers have a stable skeleton and are easily prepared in one stage on a scale of 1 kg (Haag et al., 2002). They have molecular weights which can reach 30,000 g/mole with a polydispersity of Mw/Mn~1.5. The dendrimeric structure statistically contains glycerol units incorporated linearly (primary and secondary OHs) and terminal 1,2 diols. The total density of functional groups reaches 13.5 mmol of OH/g of polymer approximately 30% (4.1 mmol/g) of which are easily accessible terminal 1,2 diols and which can be used directly for grafting aldehydes or ketones onto these polymers in the form of acetals. These dendritic polyglycerols have been used in SPOS for the functional arrangement of ω-halogenated ketones and for Suzuki coupling. Another problem results from their structure: the OH functions at the periphery which can be used for the synthesis are not identical, to the extent that there is a mixture of secondary and primary OHs which do not have the same reactivity and therefore lead to problems of selectivity and probably of secondary reactivity.

In spite of the different advantages presented by the soluble polymer supports currently used, the drawbacks linked to their high molecular weight and their limited usable specific charge are severe handicaps in generalized use. In fact, the PEGs most often used for organic synthesis and combinatorial chemistry on soluble supports have molecular weights comprised between 2000 and 10,000 daltons and have only a specific charge comprised between 0.1 and 1 mmol/g of polymer. ^{1}H and ^{13}C NMR

spectroscopy analysis of these polymers in solution can be carried out but presents difficulties as the signals corresponding to the protons and carbons of the PEGs have a strong intensity compared with the signals relating to the protons and carbons of the supported substrate. Problems of viscosity of the solutions are also encountered at high concentrations. The problems of purification of these polymers are also a severe limitation to their use and to their recycling, in particular with respect to automation of the syntheses.

For the last few years, certain onium salts referred to as "ionic liquids" (Welton et al., 1999; Wasserscheid et al., 2000; Wasserscheid and Welton, 2003), with an appropriate choice of anions, are increasingly used in organic synthesis and in catalysis as they have a certain number of useful and significant physico-chemical properties such as their great thermal stability, their low volatility and their very low vapour pressure, their low flammability, their high solubilization power both of the salts and the neutral organic molecules and the polymers and finally the possibility of easy recycling.

However, the onium salts described in the literature are generally synthesized and used as such for their biological or physical properties (surfactants for example).

The purpose of the present invention is to provide a novel use of onium salts as soluble supports for organic synthesis in homogeneous phase in the presence of at least one organic solvent.

The purpose of the present invention is to provide novel soluble supports for organic synthesis in the presence of at least one solvent, by replacing the soluble supports of the prior art such as PEGs, said novel soluble supports being easier to prepare, use and purify, perfectly defined and identified, less expensive and easy to functionalize.

The purpose of the present invention is to provide novel soluble supports having a high specific charge, the recycling of which is easy.

The present invention relates to the use of an onium salt functionalized by at least one organic function, as a soluble support, in the presence of at least one organic solvent, for the organic synthesis of a molecule, in homogeneous phase, by at least one conversion of said organic function, said onium salt allowing the release of the synthesized molecule,

said onium salt being presented in liquid or solid form at ambient temperature, and corresponding to the formula A_1^+, X_1^-,

in which: – A_1^+ represents a cation,

– X_1^- represents an anion,

A_1^+ being a functional or polyfunctional cation, and/or

X_1^- being a functional or polyfunctional anion,

the onium salt being as in its initial form, i.e. before the first conversion of said organic function, A_1^+ and X_1^- are not bound together by a covalent bond,

and when the anion and the cation respectively carry an organic function, these cannot react with each other before the first conversion of said organic function.

The use as a soluble support, i.e. in solution in a solvent or a mixture of solvents, of onium salts is demonstrated within the scope of the invention. This was not a priori evident given the knowledge about these salts. In the form of halides, they are generally not very soluble in the usual solvents used in organic chemistry. Moreover, their functionalization can, a priori, pose problems of chemoselectivity because of the presence of a positively charged onium group which is subject to β-elimination or to deprotonation in α position in basic medium.

The expression "functionalized onium salt" designates the ammonium, phosphonium, sulphonium salts, as well as all the salts resulting from the quaternization of an amine, phosphine, arsine, thioether or of a heterocycle containing one or more of these heteroatoms, and carrying at least one organic function F_i or F'_i. This expression also designates an onium salt the cation of which as defined above is not functionalized but the anion of which carries a function F'_i. This expression can also designate a salt the anion and the cation of which carry at least one organic function.

The expression "soluble support" designates a functional polymer molecule or a salt serving as "anchor" in order to carry out, in solution, successive conversions of a molecule attached by the function. This anchor confers properties to the attached molecule (therefore finally to the assembly formed by the anchor and the attached molecule) which allow easy purification by washing, evaporation or any other technique. This could not be done easily with molecules which are volatile and/or soluble in the usual solvents for example. By using this technique, it is possible to use an excess of reagents, for example, as in the case of insoluble Merrifield resins. A soluble support must by definition be soluble in a solvent. This confers the advantage of carrying out the reactions in solution and being able to monitor their progress using analysis techniques in a standard fashion used in the field of organic chemistry. A

soluble support must also be recoverable at the end of the conversions. In other words, the molecules synthesized on this support must be able to be easily released. Moreover, the skeleton of the soluble support must not react with the reagents used, the reactions taking place selectively on the functions attached to the basic skeleton.

The expression "organic synthesis of a molecule in homogeneous phase" designates the conversion or conversions of the chemical function or functions carried by said onium salt, followed by a cleavage reaction releasing the sought molecule in solution in a given solvent or in a mixture of solvents and the starting salt or a recyclable salt in the starting support.

The expression "functional cation" designates a molecular group which possesses at least one chemical function, as well as a head carrying a positive charge.

The expression "functional anion" designates a molecular group which possesses at least one function chemical, as well as a head carrying a negative charge.

The abovementioned onium salts are solubilized in an organic solvent or in a mixture of organic solvents then brought into the presence of an excess or non-excess of reagent. They are then used as soluble supports . Another property of these salts is that they are not soluble in certain usual solvents such as ether, alkanes or hydrocarbons for example. Moreover, they have extremely low vapour pressures and can therefore be placed under a high vacuum without losses. These two properties allow the use of an excess of reagent which is then easily eliminated by washing, by extraction or under high vacuum as in the case of reactions on resins or on PEG. A large number of chemical conversions of the functional onium salts are possible. These salts can be used as resins or soluble polymers.

The specific charge of a support is defined by the quantity of reagent which can be supported per gram of support and is expressed in mmol/g. This in fact corresponds to what could be called the specific functionality of a support denoted f which can be expressed in millifunctions per gram (mf/g). If the salt is monofunctional, the specific functionality (f expressed in mf/g) is equal to the specific charge expressed in mmol/g. If the salt carries n times the same function, the specific functionality f is equal to n times the specific charge x of the salt. When the onium salts are in solution, which is practically always the case, the concepts defined above must be adapted. The molarity of a solution is expressed in mol/l or in mmol/ml. Knowing the density of the solutions, it is then easy to convert to mmol/g of solution thus producing precise elements on the

specific charge of the solutions for comparison with Merrifield resins or the solutions of polymer-type soluble supports (PEG or others).

If the salt carries n times the same function, a solution containing for example a millimole of this salt per gram has a specific functionality ***f*** of n mf/g.

The monofunctionalized onium salts as used within the scope of the present invention have a specific charge greater than 1 $mmol.g^{-1}$ and are able to reach up to 7 $mmol.g^{-1}$, compared to that of PEG 5000 which is 0.2 $mmol.g^{-1}$.

The expression "conversion of the organic function" designates the modification of a function F_i by one or more reagents and/or catalysts and/or by physical activation (heating, micro-waves, ultrasound, hν radiations, pressure, electrochemistry etc.).

The expression "onium salt in its initial form" designates the salt in which the initial organic function has not yet undergone conversion, i.e. has not yet been involved in a reaction, this function being hereafter designated F_0.

The expression "first conversion of the organic function" designates the modification of the initial organic function carried by the onium salt in its initial form, which is symbolized hereafter by the modification of F_0 to F_1.

A salt in which the cation and the anion respectively carry an initial organic function named F_0 and F'_0, and in which the anion and the cation do not react together before the first conversion of said organic functions, is a salt in which the functions F_0 and F'_0 are chemically compatible or also chemically inert in relation to each other. This therefore means that the salt in question is stable. F_0 and F'_0 can on the other hand react together under the effect of any activation which can be physical (hν radiations, micro-waves, pressure, heating etc.) or chemical (catalyst, other reagent etc.)

This novel fashion of carrying out supported synthesis is also called **OSSOS** (**O**nium **S**alt **S**upported **O**rganic **S**ynthesis).

An advantageous use according to the invention is characterized in that the onium salt is purified and/or recycled in its initial form after the release of the synthesized molecule.

The preferred processes for purification and/or recycling used are in particular a simple process of washing or recrystallization from an appropriate solvent.

An advantageous use of the present invention is characterized in that the functional cations and anions correspond to an ionic entity, cationic Y^+– and anionic Z^- – respectively, optionally bound by means of an arm, L and M respectively, in particular

an alkyl or aralkyl or alkaryl group comprising 1 to 30 carbon atoms, to at least one function F_i and F'_i respectively, F_i varying from F_0 to F_n, F'_i varying from F'_0 to F'_n, n being an integer varying from 1 to 20,

the functional cation A_1^+ being able to be represented in the form $Y^+–L–F_i$, and

the functional anion X_1^- in the form $Z^-–(M)_k–F'_i$, k being equal to 0 or 1.

The expression “ionic entity” designates the part of the cation or anion which carries the charge, positive or negative respectively.

The functions F_i and F'_i are in particular chosen from the following functions:

hydroxyl, carboxylic acid, amide, sulphone, primary amine, secondary amine, aldehyde, ketone, ethenyl, ethynyl, dienyl, ether, epoxide, phosphine (primary, secondary or tertiary), azide, imine, ketene, cumulene, heterocumulene, thiol, thioether, sulphoxide, phosphorated groups, heterocycles, sulphonic acid, silane, stannane or functional aryl, and any function resulting from a conversion of the preceding functions by chemical route or induced by thermal, electrochemical, photochemical activation or by any other physical technique such as micro-wave irradiation, ultrasound or pressure.

In the term “Y^+–”, the dash “–” represents the optional bond between the cationic entity and the L arm.

In the term “Z^-–”, the dash “–” represents the optional bond between the anionic entity and the L arm.

The term “L arm” designates an alkyl or aralkyl or alkaryl chain which can contain one or more heteroatoms such as nitrogen, phosphorus, sulphur, oxygen, silicon, tin, containing between 1 and 30 carbon atoms, and said arm is in particular chosen from an alkyl chain containing from 2 to 20 carbon atoms and from 1 to 6 of oxygen nitrogen atoms.

According to an advantageous embodiment, the functionalized onium salt A_1^+, X_1^- used within the scope of the present invention is soluble in a organic solvent.

According to an advantageous embodiment, the functionalized onium salt A_1^+, X_1^- used within the scope of the present invention is liquid at ambient temperature.

According to an advantageous embodiment, the onium salt A_1^+, X_1^- used within the scope of the present invention is solid at ambient temperature and can be liquefied within a range of temperatures ranging from approximately 25°C to approximately 450°C, in particular from approximately 30°C to approximately 150°C.

An advantageous use of the invention is characterized in that the organic functions F_i and F'_i are chosen from the standard functions of organic chemistry, such as the hydroxyl functions, carboxylic acid, amide, sulphone, primary amine, secondary amine, aldehyde, ketone, ethenyl, ethynyl, dienyl, ether, epoxide, phosphine (primary, secondary or tertiary), azide, imine, ketene, cumulene, heterocumulene, thiol, thioether, sulphoxide, phosphorated groups, heterocycles, sulphonic acid, silane, stannane or functional aryl.

An advantageous use of the present invention is characterized in that the molecular weight of the functionalized onium salt is less than 1500 $g.mol^{-1}$, in particular less than 750 $g.mol^{-1}$, and is preferably comprised from 130 to 500 $g.mol^{-1}$.

In order to ensure a good productivity of the support, it is necessary for the molecular mass of the salt to be as low as possible (owing to the specific charge as defined previously). Thus, anions with the lowest possible mass, such as the chlorides, are preferably used in order to be able to optionally use cations with a higher mass (see Table 17 below representing the variations in specific charge as a function of mass).

An advantageous use of the present invention is characterized in that A_1^+ is a functional cation and in that X_1^- is a non-functional anion.

The expression "non-functional anion" designates a molecular group which does not possess any chemical function, part of this group carrying a negative charge.

This embodiment makes it possible to carry out specific reactions on the cationic part of the onium salt. It is therefore possible to control the selectivity and the reactivity which could be different on the anion and the cation.

The present invention also relates to a use as defined above, in which the onium salt A_1^+, X_1^- has as its initial form $Y^+–L–F_0$, X_1^-, for obtaining a molecule G, by conversion of said initial function F_0 according to the diagram

$$\overset{+}{Y}\text{-}L\text{-}F_0\,,\ \overset{-}{X_1} \longrightarrow \overset{+}{Y}\text{-}L\text{-}F_i\,,\ \overset{-}{X_1} \longrightarrow \cdots \longrightarrow \overset{+}{Y}\text{-}L\text{-}F_n\,,\ \overset{-}{X_1} \longrightarrow G + \overset{+}{Y}\text{-}L\text{-}F_0\,,\ \overset{-}{X_1}$$

L being as defined above,

said molecule G being obtained by cleavage at the level of the function F_n,

and the functionalized onium salt being able to be recovered or recycled in its initial form $Y^+–L–F_0$, X_1^-, after the release of G.

The reactions used for the release of G by cleavage are in particular the following: transesterification, transamidation, reduction, lactonization, lactamization, releasing cyclization and releasing coupling.

An advantageous use of the invention is characterized in that the functional cation A_1^+ is chosen from the pyridinium, imidazolium, ammonium, phosphonium or sulphonium cations, cyclic or non-cyclic, substituted or non-substituted, and preferably ammonium or phosphonium.

An advantageous use according to the invention is characterized in that the functional cation A_1^+ is chosen from the quaternary ammonium cations, cyclic or non-cyclic.

An advantageous use according to the invention is characterized in that X_1^- is a functional anion and A_1^+ is a non-functional cation.

The expression "non-functional cation" designates a molecular group which possesses no chemical function, part of this group carrying a positive charge.

This embodiment makes it possible to carry out functional modifications only on the anionic part.

The present invention also relates to a use as defined above, in which the onium salt A_1^+, X_1^- has as its initial form A_1^+, Z^--$(M)_k$-F'_0, for obtaining a molecule G, by conversion of said initial function F'_0 according to the diagram

$$A_1^+ , Z^- - (M)_k - F'_0 \longrightarrow A_1^+ , Z^- - (M)_k - F'_i \longrightarrow \cdots \longrightarrow A_1^+ , Z^- - (M)_k - F'_n \longrightarrow G + A_1^+ , Z^- - (M)_k - F'_0$$

k and M being as defined above,

said molecule G being obtained by cleavage of the function F'_n,

and the functionalized onium salt being able to be recovered or recycled in its initial form A_1^+, Z^-–$(M)_k$–F'_0, after the release of G.

The reactions used for the release of G by cleavage are in particular the following: transesterification, transamidation, reduction, lactonization, lactamization, releasing cyclization and releasing coupling.

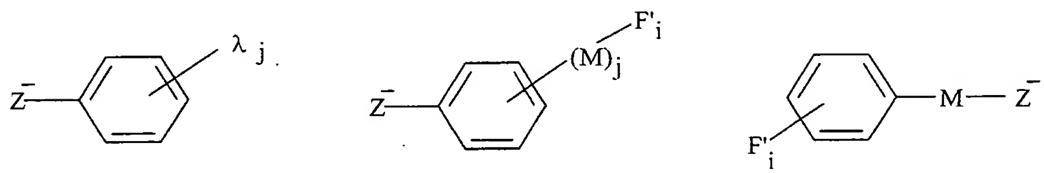
An advantageous use of the invention is characterized in that X_1^- is chosen from:

- the family of the phosphates: $R_1PO_4^{2-}$, $R_1R_2PO_4^-$,
- the family of the sulphates: $R_1SO_4^-$,
- the family of the sulphonates: $R_1SO_3^-$,

– the family of the carboxylates: $R_1CO_2^-$,

or from the following anions:

$R_1\bar{N}SO_2R_2$ $\quad$ $R_2SO_2\bar{N}SO_2R_2$ $\quad$ $R_1-\overset{\lambda}{\underset{\gamma}{C^-}}$



Z^-, M and F'_i being as defined above, Z^- representing in particular O^-, SO_3^-, CO_2^-, $R_1PO_3^-$ or $R_1PO_2^-$,

j representing an integer comprised between 1 and 5,

R_1 and R_2 being able to represent independently of one another a functional alkyl group, a vinyl or alkynyl group, optionally functional, comprising from 1 to 20 carbon atoms, or being able to represent a functional aryl group comprising from 6 to 30 carbon atoms,

γ and λ representing an electroattractive group, in particular chosen from the groups: $CO_2R'_1$, $SO_2R'_1$, CN, NO_2, $P(O)(OR'_1)_2$, $C(O)R'_1$ and $SO_3R'_1$,

R'_1 representing an alkyl group, optionally functional, comprising from 1 to 20 carbon atoms, or an aryl group, optionally functional, comprising from 6 to 30 carbon atoms.

An advantageous use according to the invention is characterized in that A_1^+ is a functional cation and X_1^- is a functional anion.

This embodiment makes it possible to carry out conversions in parallel as well as the intra- or intermolecular reaction of a function of A_1^+ with a function of X_1^-.

The present invention also relates to a use as defined above, in which the onium salt A_1^+, X_1^- has as its initial form $Y^+–L–F_0, Z^-–(M)_k–F'_0$, for obtaining a molecule G, by conversion of said initial functions F_0 and F'_0 according to the diagram

$$Y^+\!-L-F_0\ ,\ Z^-\!-(M)_k-F'_0 \longrightarrow Y^+\!-L-F_i\ ,\ Z^-\!-(M)_k-F'_i \longrightarrow \cdots \longrightarrow Y^+\!-L-F_n\ ,\ Z^-\!-(M)_k-F'_n$$

L, k and M being as defined above,

and by reaction of F_n on F'_n in the functionalized onium salt $Y^+\!-L-F_n\ ,\ Z^-\!-(M)_k-F'_n$ leading to the formation of an internal salt of formula:

$$Y^+\!-L-F_{n+1}-F'_{n+1}-(M)_k-Z^-$$

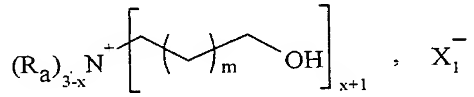
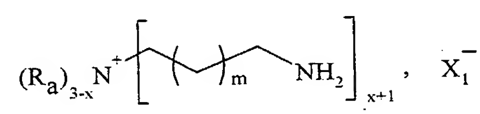
said molecule G being obtained by cleavage of the abovementioned internal salt and corresponding to the formula F_{n+2}-F'_{n+2},

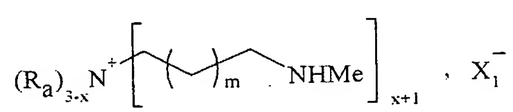
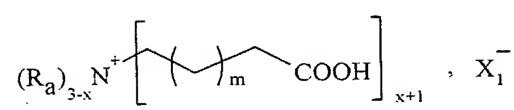
and the functionalized onium salt being able to be recovered or recycled in its initial form Y^+–L–F_0, Z^-–$(M)_k$–F'_0, after the release of G.

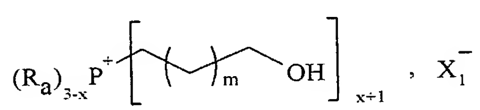
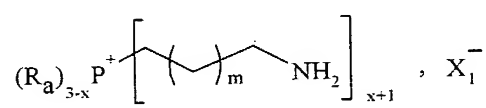
This embodiment makes it possible to carry out intramolecular reactions.

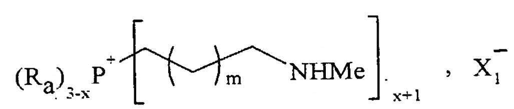
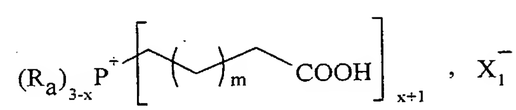
The expression "internal salt" designates an entity simultaneously carrying at least one positively charged group and one negatively charged group, separated by at least 2 atoms, linked by covalent bonds.

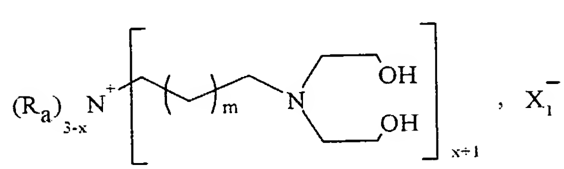
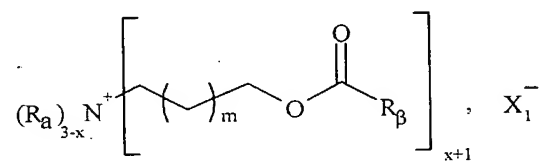
A use according to the present invention is characterized in that the onium salt is chosen from the following salts:

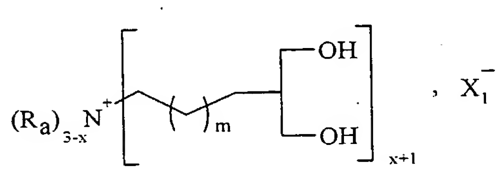
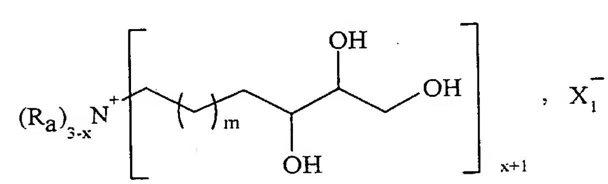



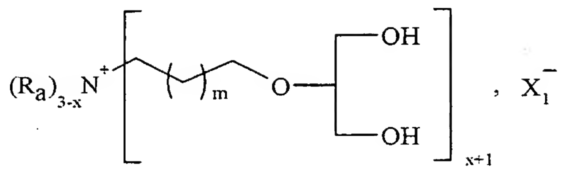



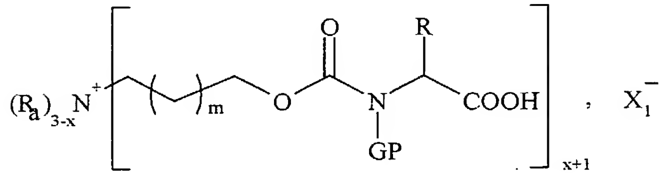



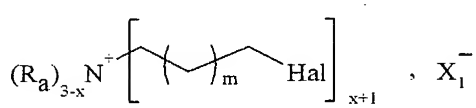



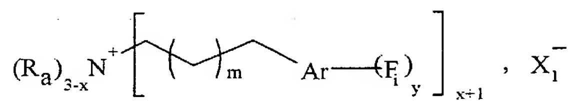



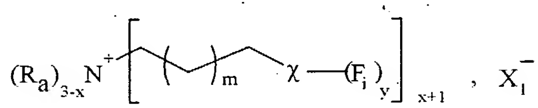













R representing a hydrogen atom, an alkyl, alkaryl or aralkyl group, functional or non-functional, comprising from 1 to 20 carbon atoms, or an aryl group, functional or non-functional, comprising from 6 to 30 carbon atoms,

x representing an integer comprised from 0 to 3,

y representing an integer comprised from 1 to 5,

Ar representing a functional or polyfunctional aromatic ring ,

F_i being as defined previously,

Hal representing a halogen atom, in particular chosen from chlorine, bromine and iodine,

χ representing a carbocycle or a functional heterocycle,

X_1^- being chosen from: NTf_2^-, PF_6^-, BF_4^-, Cl^-, Br^-, I^-, $CF_3SO_3^-$, $MeSO_4^-$, $EtSO_4^-$, $MeSO_3^-$, $C_6H_5SO_3^-$, $pMeC_6H_4SO_3^-$,

m being an integer comprised from 0 to 20,

R_β representing a dienyl, vinyl group, substituted or non-substituted, functional alkyl comprising from 1 to 20 carbon atoms, or functional aryl comprising from 6 to 30 carbon atoms, substituted or non-substituted alkynyl, and being in particular an alkylvinyl, alkylalkynyl, alkylaryl, alkyldienyl, alkylmalonyl, acyl group,

and R_a representing a branched or non-branched alkyl group comprising from 1 to 20 carbon atoms, in particular an ethyl, propyl, butyl, pentyl, hexyl, heptyl or octyl group.

The present invention also relates to a use as defined above, characterized in that the solvent or solvents used are aprotic solvents, chosen from:

– solvents the dielectric constant ε of which is less than or equal to 2, such as the alkanes, the aromatic carbides such as benzene, toluene or xylene,

– solvents the dielectric constant ε of which is comprised between approximately 2 and 15, such as the ethers, halogenobenzenes or dichloromethane, and

– solvents the dielectric constant ε of which is greater than 15, such as acetonitrile, nitromethane, DMF or dimethylacetamide.

The dielectric constant ε and/or the dipole moment are often used to characterize the polarity of a solvent. More recently, the Dimroth-Reichardt parameter E_T^N has been proposed in order to better describe the polarity of the solvents (Reichardt, 1988).

The solvents advantageously used in the invention are toluene, dichloromethane, THF, acetonitrile and DMF.

The present invention also relates to a use as defined above, for continuous, discontinuous, combinatorial or parallel organic synthesis, and/or for the preparation of banks of products.

The advantages of the use of the abovementioned onium salts are the following:

– a large number of functional onium salts are known, which are easily accessible and certain of which are commercial;

– the functional modifications of the onium salts are generally simple and easy to carry out according to methods described in the literature; if they do not exist, they can be worked out from knowledge of organic chemistry;

– the reactions take place in homogeneous phase, which means that any knowledge of reactivity in organic, organometallic and catalytic chemistry is applicable; moreover, all analysis techniques, including ^{1}H, ^{13}C, ^{19}F, ^{31}P, ^{11}B, ^{15}N NMR etc., HPLC, IRTF, UV-visible, fluorescence, electrochemical techniques, electrophoresis, mass spectrometry etc., can be used under normal conditions without particular complications;

– the reactions are carried out at the usual concentrations of 0.5 to 1 mole per litre (or even much more) which represents a huge advantage in terms of specific charge;

– purification of the intermediates is generally easy;

– the recycling of these supports is easy;

– the solutions of salts in the usual solvents are easily transferable using syringe and/or pumping techniques;

– the solutions of onium salts in the organic solvents easily lend themselves to partition techniques and therefore to parallel or combinatorial synthesis techniques; libraries of products can therefore be easily synthesized;

– the reactivities and selectivities depend on the nature of the anion or the cation;

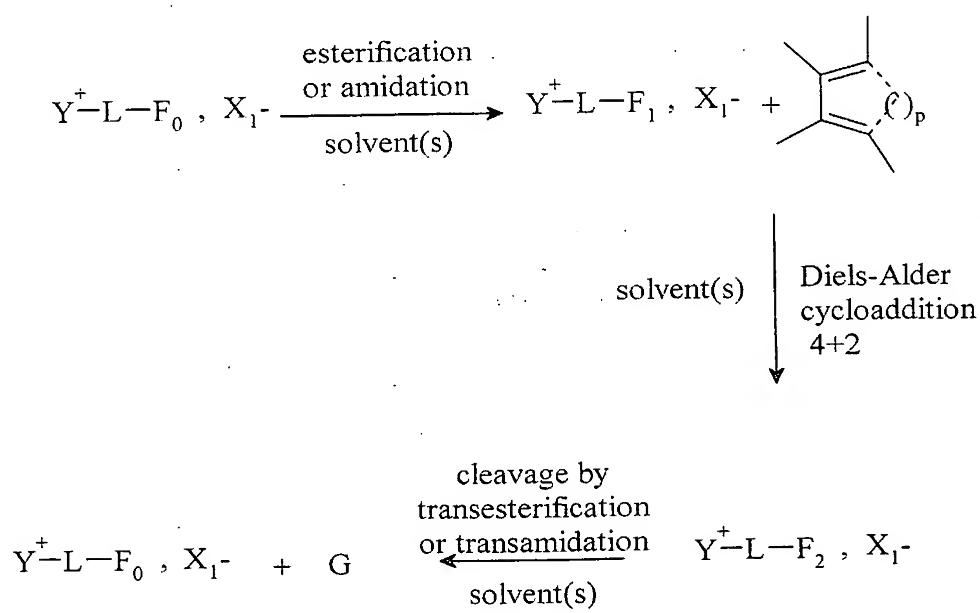
– scaling-up does not pose any problems, which is a major advantage compared with resins and soluble polymers;

– an analogy is easily established between this novel technology and synthesis techniques on Merrifield-type resins or soluble polymers of PEG, PG or JANDA type; these onium salts can be functionalized as Wang, Rink, silylalkyl, carbonate, carboxylic, formyl, hydroxyl, amino, oxime resins etc. or the functionalized polymers but are much easier and more advantageous to use;

– they are much less expensive; this economic advantage is very important, being of a kind to open up a large substitution market.

The present invention also relates to a use as defined above, for the implementation of cycloaddition reactions, preferably for the implementation of the Diels-Alder reaction, according to one of the following reaction diagrams:

a)



p being an integer varying from 0 to 2,

Y^+– representing an onium cation as defined previously, and preferably being a trimethylalkylammonium, triethylalkylammonium, tributylalkylphosphonium, N-methylimidazolium or pyridinium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group, comprising from 6 to 30 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 2 to 10,

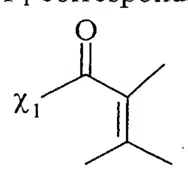
X_1^- being as defined previously, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

the functions F_0, F_1 and F_2 being as defined below:

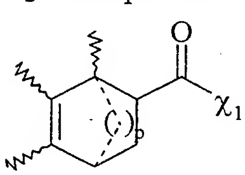
– F_0 corresponds to a $-\chi_1H$ group, in which χ_1 represents an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

– F_1 corresponds to the following formula:



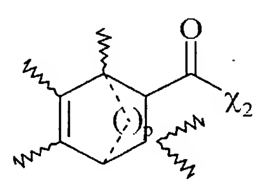
χ_1 being as defined above,

– F_2 corresponds to the following formula:



χ_1 being as defined above,

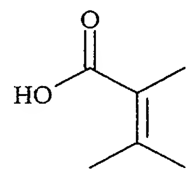
G corresponding to the following formula:



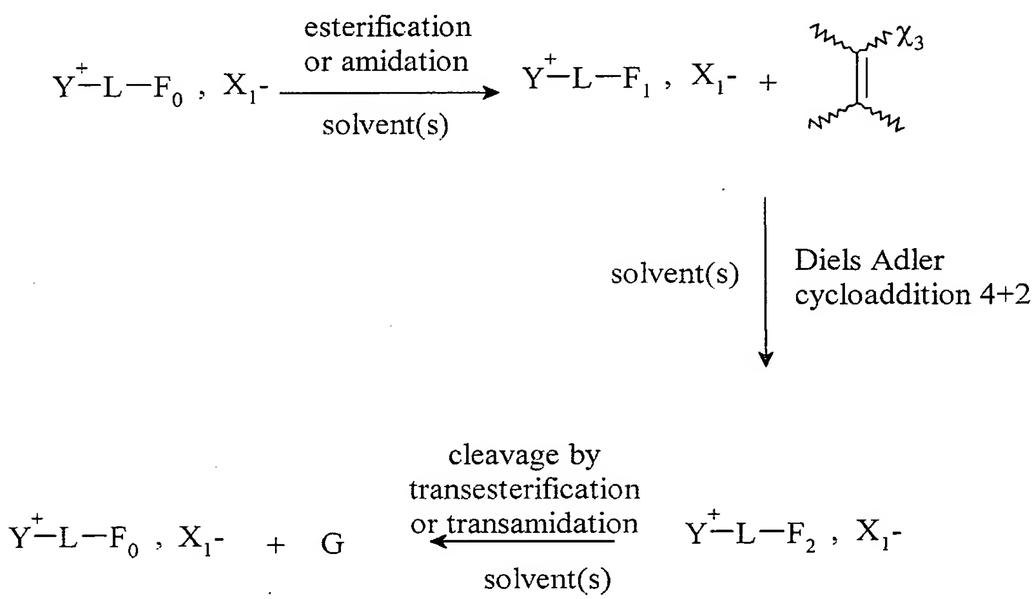
in which χ_2 represents either an OR_g group, R_g representing a hydrogen atom or an alkyl group comprising from 1 to 20 carbon atoms, or an $-NR_hR_u$ group, R_h and R_u

representing independently of one another a hydrogen atom, an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms,

the esterification or amidation reaction in this reaction diagram being carried out by adding carboxylic acid of the following formula:



b)



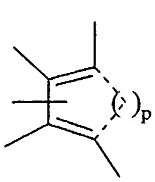
Y^+–, L and X_1^- being as defined previously,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, or a mixture of these solvents,

the functions F_0, F_1 and F_2 being as defined below:

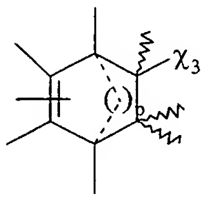
– F_0 represents any function making it possible to attach a 1,3-diene, and is in particular chosen from the carbonyl, amine, alkoxy, silane, stannane and borane functions, comprising from 1 to 20 carbon atoms,

– F_1 corresponds to the following formula:



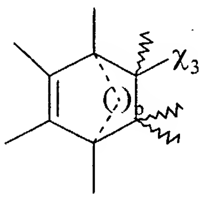
p being an integer varying from 0 to 2,

– F_2 corresponds to the following formula:



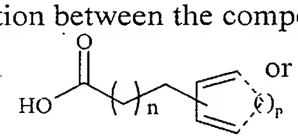
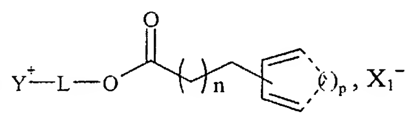
χ_3 representing an electroattractive group, in particular chosen from the cyano, alkoxycarbonyl groups, comprising from 1 to 20 carbon atoms, acyl comprising from 2 to 20 carbon atoms, benzoyl, sulphonyl, dialkoxyphosphonyl comprising from 1 to 10 carbon atoms,

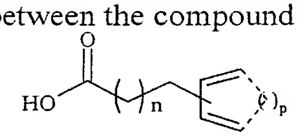
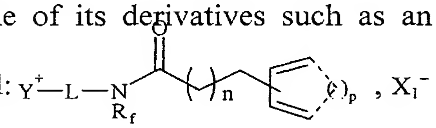
G corresponding to the following formula:

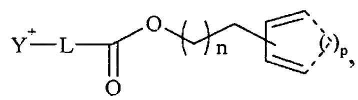
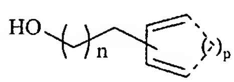


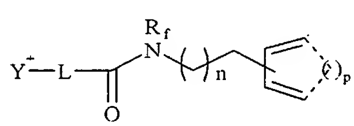
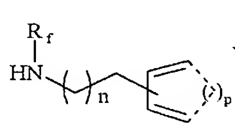
χ_3 being as defined above.

The passage from F_0 to F_1 is carried out as follows:

– by esterification between the compound of formula $\overset{+}{Y}-L-OH$ X_1^- and the compound of formula  or one of its derivatives such as an acid chloride in order to obtain the following compound: 

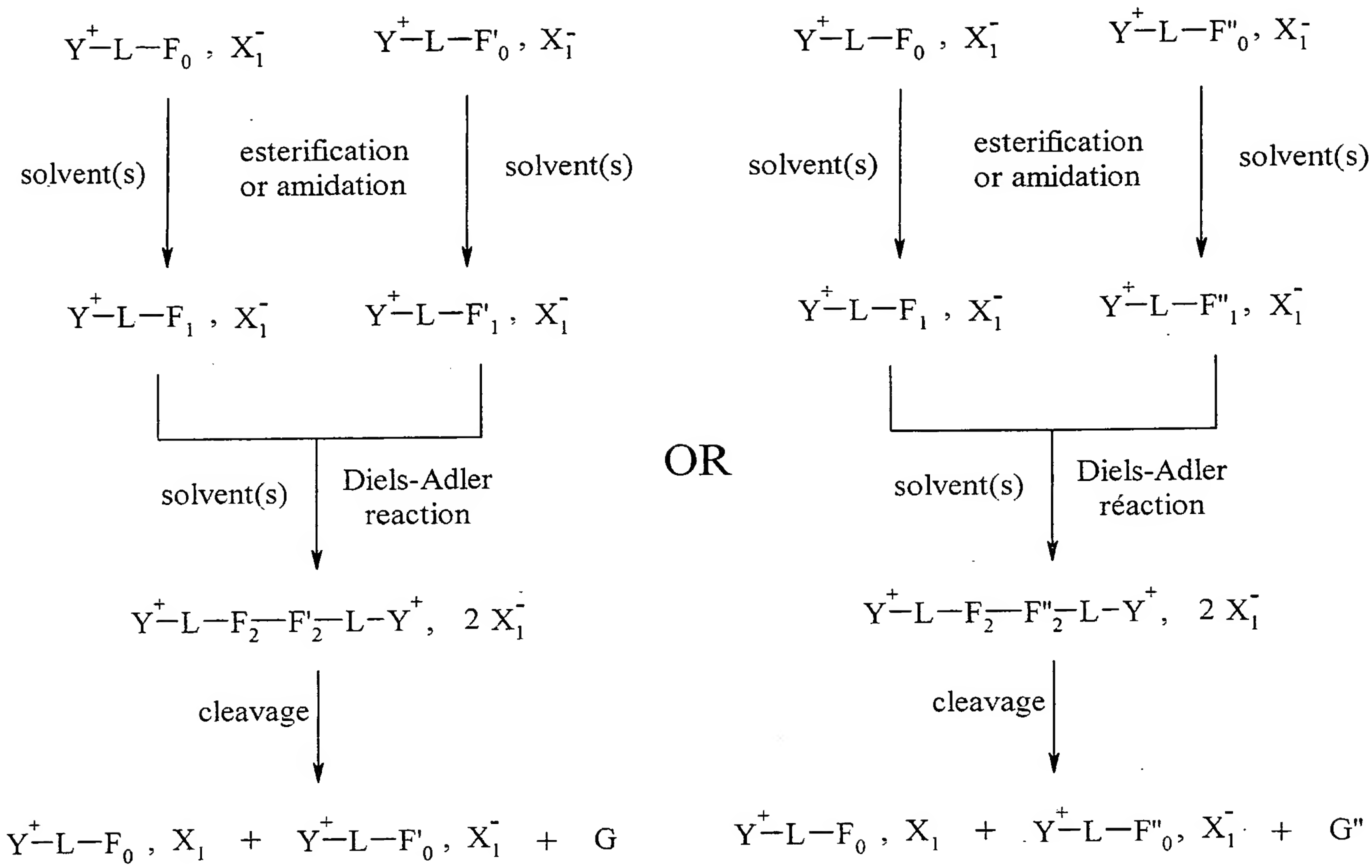
– by acylation between the compound of formula $\overset{+}{Y}-L-\underset{R_f}{NH}$, X_1^- and the compound of formula  or one of its derivatives such as an acid chloride in order to obtain the following compound: 

The product of formula  is obtained by esterification of alcohols of formula  with $\overset{+}{Y}-L-COOH$, X_1^- or $\overset{+}{Y}-L-COCl$, X_1^-

The product of formula  is obtained by acylation of the amines of formula  with $\overset{+}{Y}-L-COOH$, X_1^- or $\overset{+}{Y}-L-COCl$, X_1^-

n, R_f, p, X_1^-, Y and L being as defined previously,

c)



Y^+–, L and X_1^- being as defined previously,

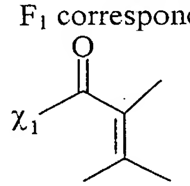
the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

the functions F_0, F'_0, F''_0, F_1, F'_1, F''_1, F_2, F'_2 and F''_2 being as defined below:

– F_0 and F'_0 correspond respectively to a $-\chi_1H$ and $-\chi'_1H$ group, in which χ_1 and χ'_1, identical or different, represent an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

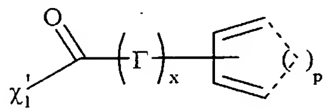
– F''_0 corresponds to a -COOH function;

– F_1 corresponds to the following formula:



χ_1 being as defined above,

– F'_1 corresponds to the following formula:



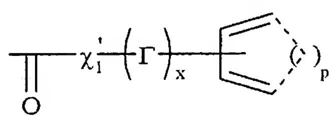
p being an integer varying from 0 to 2,

χ'_1 being as defined above,

x being equal to 0 or 1,

Γ representing an alkyl chain comprising from 1 to 30 carbon atoms, alkaryl, aralkyl, aryl comprising from 6 to 30 carbon atoms,

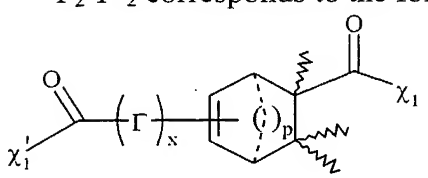
– F''_1 corresponds to the following formula:



p, x and Γ being as defined above,

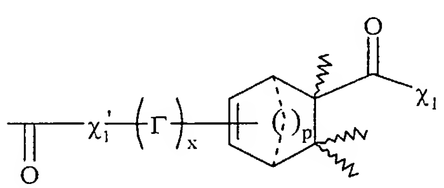
χ'_1 being as defined above,

– F_2-F'_2 corresponds to the following formula:



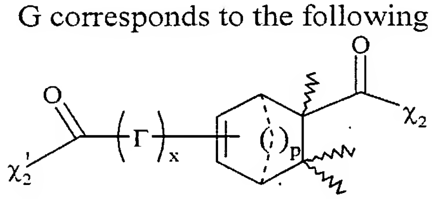
p, χ_1, χ'_1, x and Γ being as defined above,

– F_2-F''_2 corresponds to the following formula:

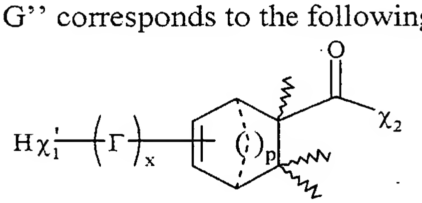


p, χ_1, χ'_1, x and Γ being as defined above,

– G corresponds to the following formula:



– G'' corresponds to the following formula:

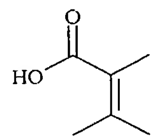


χ_2 and χ'_2, identical or different, represent either an OR_g group, R_g representing a hydrogen atom or an alkyl group comprising from 1 to 20 carbon atoms, or an $-NR_hR_u$ group, R_h and R_u representing independently of one another a hydrogen atom, an alkyl

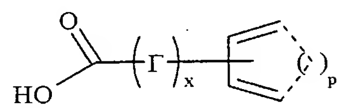
group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms.

In the last reaction diagram (case c):

– the passage from F_0 to F_1 is carried out by esterification or amidation of the carboxylic acid of formula

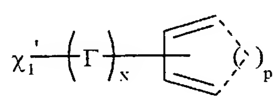


– the passage from F'_0 to F'_1 is carried out by esterification or amidation of the carboxylic acid of formula



Γ, x and p being as defined above,

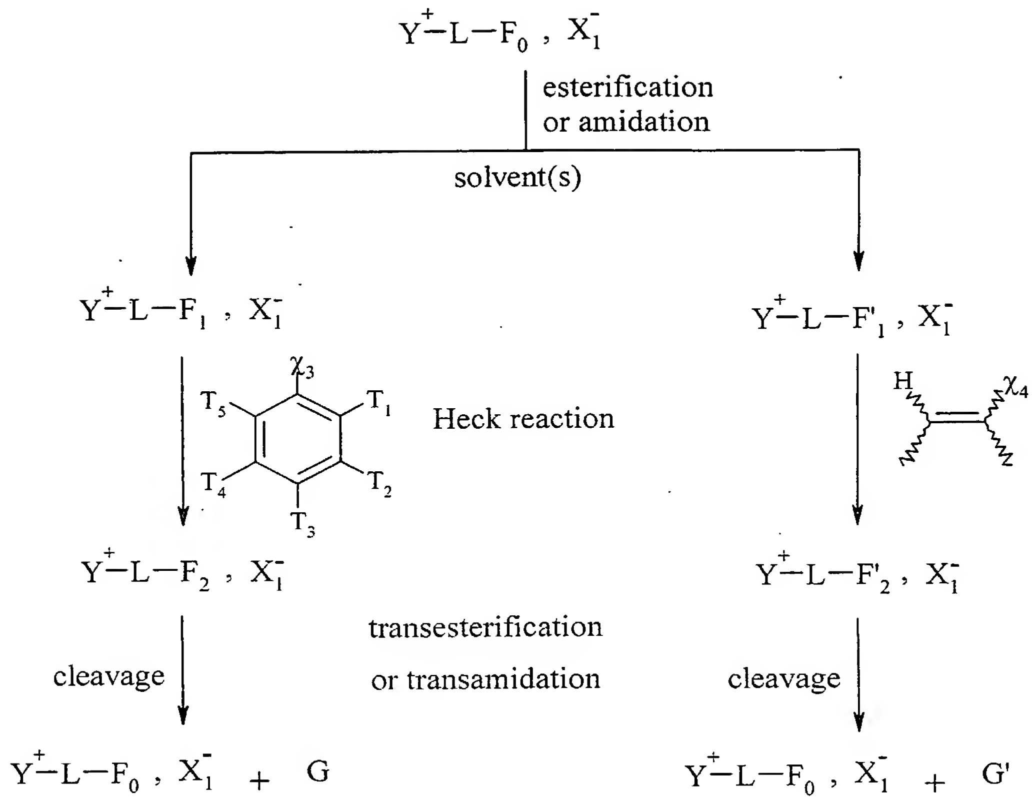
– the passage from F''_0 to F''_1 is carried out by the addition of the compound of formula



Γ, x, p and χ'_1 being as defined above.

The present invention relates to the use as defined above, for the implementation of coupling reactions such as the Heck, Suzuki, Sonogashira or Ullmann reactions.

The present invention also relates to the use as defined above for the implementation of the Heck reaction, according to one of the following reaction diagrams:



Y^+– representing an onium cation as defined above, and preferably being a trimethylalkylammonium, triethylalkylammonium, tributylalkylphosphonium, tricyclohexylalkylphosphonium, N-methyl-N'-alkylimidazolium, N-alkylpyridinium, dimethylalkylsulphonium, diethyl-alkylsulphonium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group, comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 2 to 10,

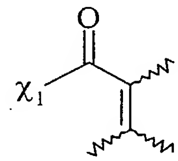
X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

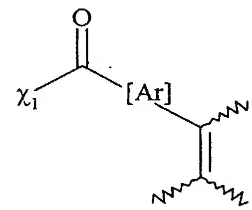
the functions F_0, F_1, F'_1, F_2 and F'_2 being as defined below:

– F_0 corresponds to a $-\chi_1H$ group, in which χ_1 represents an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

– F_1 corresponds to one of the following formulae:

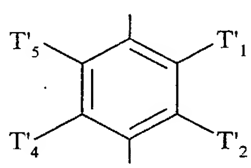


or



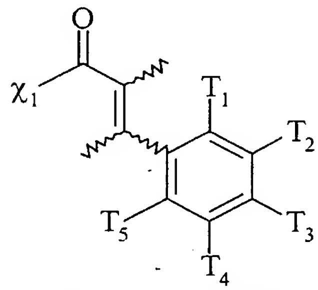
χ_1 being as defined above,

[Ar] representing an aromatic ring, optionally substituted by a linear or branched alkyl group, comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms, or a functional group in particular chosen from NO_2, CN, COOR, OR, COR, NHCOR, NRR', SO_2R, I, Br, R and R' representing independently of one another an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms, [Ar] preferably corresponding to the following formula:

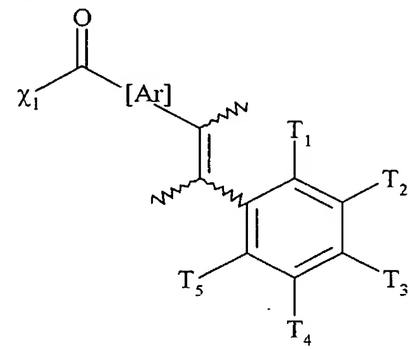


in which T'_1, T'_2, T'_4 and T'_5 represent independently of one another a hydrogen atom, a linear or branched alkyl group, comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms, or a functional group in particular chosen from NO_2, CN, COOR, OR, COR, NHCOR, NRR', SO_2R, I, Br, R and R' representing independently of one another an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms,

– F_2 corresponds to one of the following formulae:



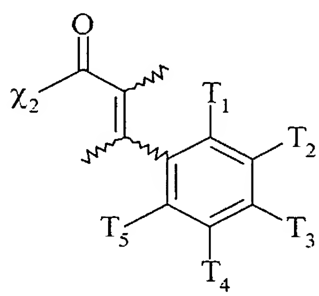
or



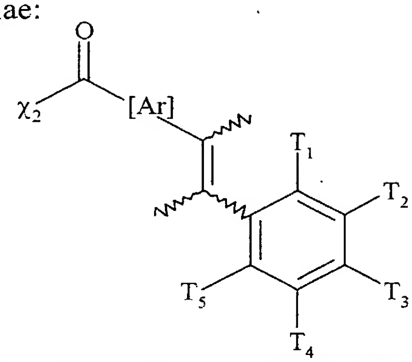
χ_1 and Ar being as defined above,

T_1, T_2, T_3, T_4 and T_5 corresponding to the definition given above for T'_1, T'_2, T'_4 and T'_5

G corresponding to one of the following formulae:

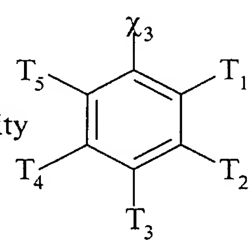


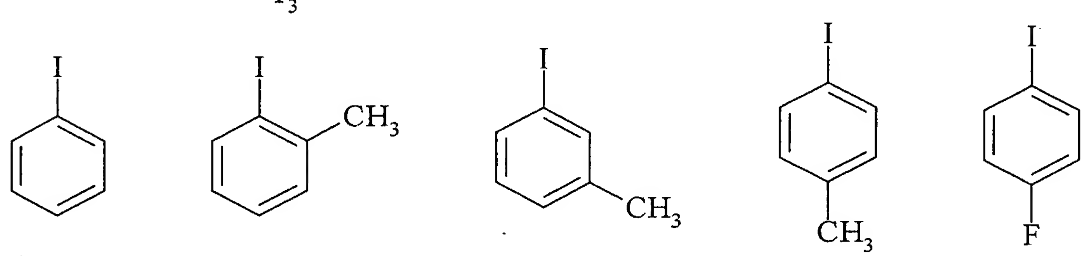
or

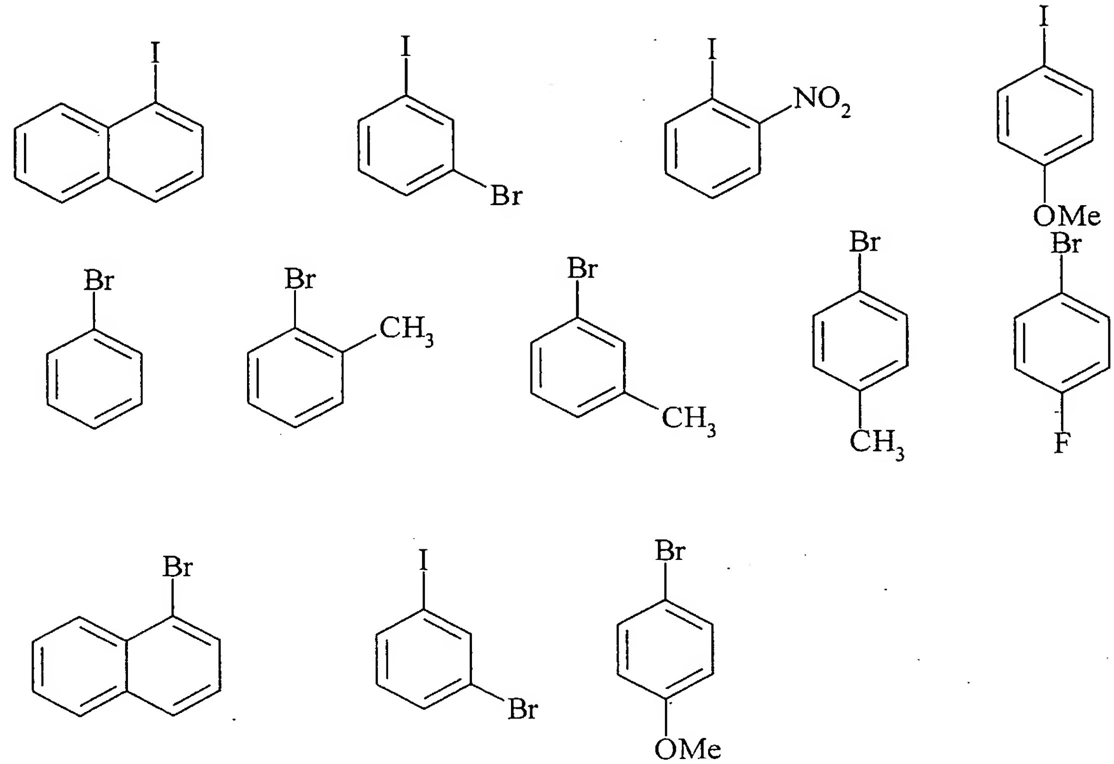


in which χ_2 represents either an $-OR_g$ group, R_g representing a hydrogen atom or an alkyl group comprising from 1 to 20 carbon atoms, or an $-NR_hR_u$ group, R_h and R_u representing independently of one another a hydrogen atom, an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms,

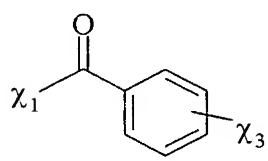
χ_3 representing a leaving group, in particular chosen from the I, Cl and Br halides, the mesylate, tosylate, triflate, sulphonate, sulphate or phosphate groups,

the entity  representing in particular the following groups:



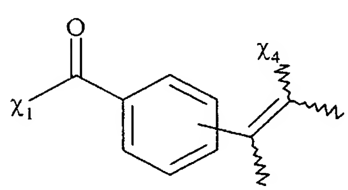


– F'₁ corresponds to the following formula:



χ_1 and χ_3 being as defined above,

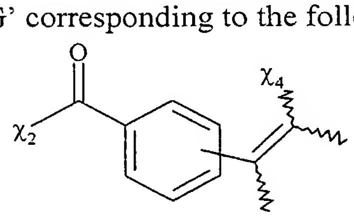
– F'₂ corresponds to the following formula:



χ_1 being as defined above,

χ_4 representing a functional group of ester, amide, sulphone, phosphonate, silane, borane type, or a functional or non-functional alkyl group, comprising from 1 to 20 carbon atoms, or a functional or non-functional aryl group, comprising from 6 to 30 carbon atoms,

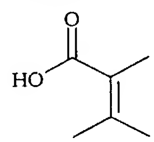
G' corresponding to the following formula:



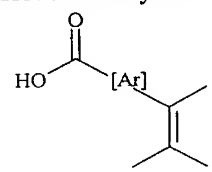
χ_2 and χ_4 being as defined above.

The left-hand part of the above reaction diagram corresponds to the binding of the acrylic radical to the support and the right-hand part of the above diagram corresponds to the binding of the arylic radical to the support.

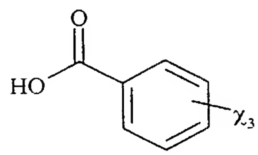
The passage from F_0 to F_1 is carried out by the esterification of the carboxylic acid of formula



or



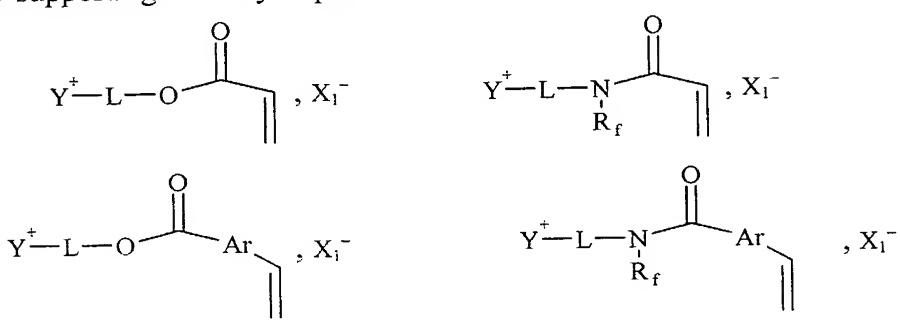
The passage from F'_0 to F'_1 is carried out by the esterification of the carboxylic acid of formula



χ_3 being as defined above.

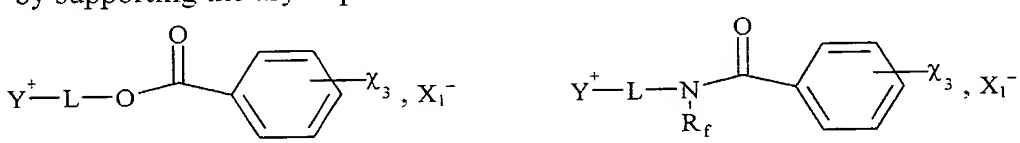
The Heck reaction can be carried out in three different fashions:

– by supporting the acrylic part as follows:



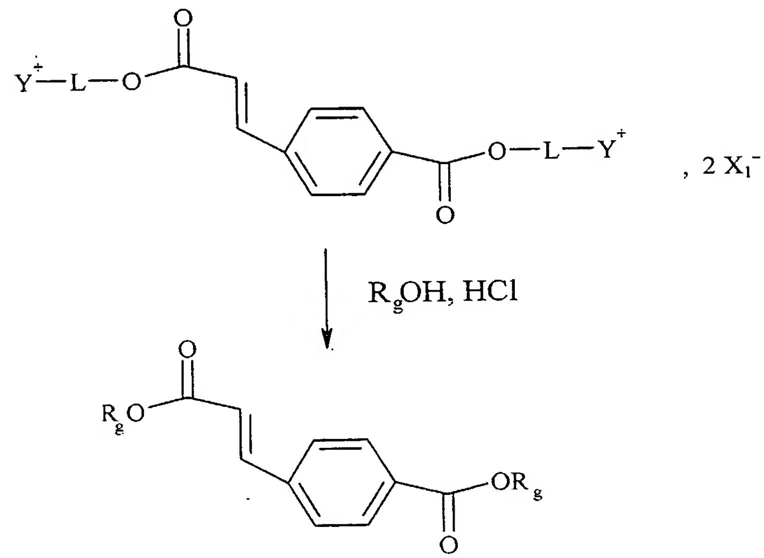
Y^+–, X_1^-, L, Ar and R_f being as defined above,

– by supporting the arylic part as follows:



Y^+–, X_1^-, L, R_f and χ_3 being as defined above,

– by supporting the acrylic and arylic parts as follows:



Y^+–, X_1^-, L and R_g being as defined above.

The present invention also relates to the use as defined above for the implementation of Suzuki coupling, according to one of the following reaction diagrams:

a)

$$\overset{+}{Y}\!-\!L\!-\!F_0\ ,\ X_1^- \xrightarrow[\text{solvent(s)}]{\text{esterification or amidation}} \overset{+}{Y}\!-\!L\!-\!F_1\ ,\ X_1^-$$

$$\downarrow \text{solvent(s)} \quad \text{Suzuki reaction with } R_3B(OR_7)_2$$

$$\overset{+}{Y}\!-\!L\!-\!F_0\ ,\ X_1^- \ +\ G \xleftarrow[\text{solvent(s)}]{\text{cleavage by transesterification or transamidation}} \overset{+}{Y}\!-\!L\!-\!F_2\ ,\ X_1^-$$

R_3 being chosen from the aryl, heteroaryl, ethenyl, dienyl, allyl, ethynyl groups, substituted or non-substituted, comprising from 2 to 30 carbon atoms,

R_7 representing a hydrogen atom or a branched or linear alkyl group, or a cycloalkyl group comprising from 1 to 12 carbon atoms,

Y^+– representing an onium cation as defined above, and preferably being a trimethylalkylammonium, triethylalkylammonium, tributylalkylphosphonium, N-methylimidazolium or pyridinium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl group comprising from 6 to 30 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 1 to 10,

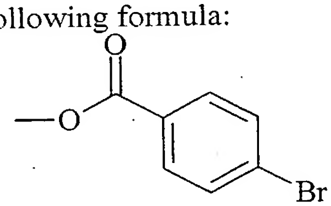
X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

the functions F_0, F_1 and F_2 being as defined below:

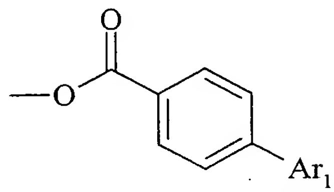
– F_0 is in the form $-\chi_1H$, χ_1 representing an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

– F_1 is in the form $-R_e-\chi$, R_e representing an aromatic or heteroaromatic group comprising from 6 to 30 carbon atoms, χ representing a leaving group preferably chosen from Cl, Br, I, OTf, $O\text{-}CO_2R^5$ or $OSO_3\text{-}R^5$, R^5 representing an alkyl group comprising from 1 to 10 carbon atoms or an aralkyl group comprising from 6 to 30 carbon atoms, F_1 preferably corresponding to the following formula:

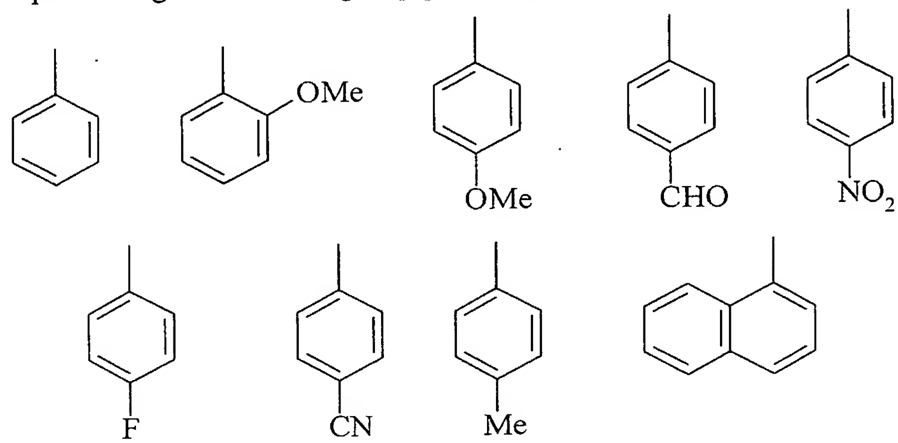


– F_2 is in the form $-R_e-R_2$, R_e being as defined above and R_2 being chosen from the aryl, heteroaryl, ethenyl, dienyl, allyl, ethynyl groups, substituted or non-substituted,

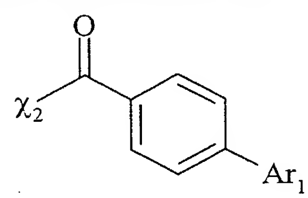
comprising from 2 to 30 carbon atoms, F_2 preferably corresponding to the following formula:



Ar_1 representing an aromatic group preferably chosen from:



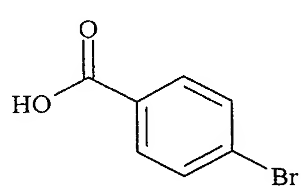
the molecule G being in the form R_2–R_3, R_2 and R_3 being as defined above, and corresponding in particular to the following formula:

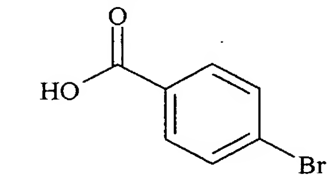


in which χ_2 represents either an $-OR_g$ group, R_g representing a hydrogen atom or an alkyl group comprising from 1 to 20 carbon atoms, or an $-NR_hR_u$ group, R_h and R_u representing independently of one another a hydrogen atom, an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms,

Ar_1 is as defined above.

When F_0 represents an -OH group, the function F_1 is obtained by esterification in particular with the carboxylic acid of formula



When F_0 represents an $-NR_fH$ group, the function F_1 is obtained by amidation in particular with the carboxylic acid of formula 

b)

$$Y^{+}\!-L-F_0\ ,\ X_1^- \xrightarrow[\text{solvent(s)}]{\text{esterification or amidation}} Y^{+}\!-L-F_1\ ,\ X_1^-$$

$$\downarrow \text{solvent(s)} \quad \text{Suzuki reaction with } R_2\chi$$

$$Y^{+}\!-L-F_0\ ,\ X_1^- \ +\ G \xleftarrow[\text{solvent(s)}]{\text{cleavage by transesterification or transamidation}} Y^{+}\!-L-F_2\ ,\ X_1^-$$

Y^+- representing an onium cation as defined above, and preferably being a trimethylalkylammonium, triethylalkylammonium, tributylalkylphosphonium, N-methylimidazolium or pyridinium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl group comprising from 6 to 30 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 1 to 10,

X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

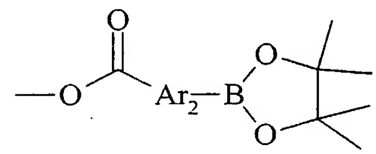
the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

R_2 being chosen from the aryl, heteroaryl, ethenyl, dienyl, allyl, ethynyl groups, substituted or non-substituted, comprising from 2 to 30 carbon atoms,

the functions F_0, F_1 and F_2 being as defined below:

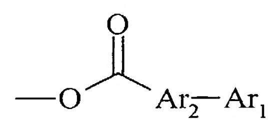
- F_0 is in the form $-\chi_1H$, χ_1 being as defined above,

– F_1 is in the form $-R_q-B(OR_7)_2$, R_7 being as defined above, and R_q corresponding to an aryl group comprising from 6 to 30 carbon atoms, heteroaryl comprising from 4 to 20 carbon atoms, ethenyl comprising from 2 to 20 carbon atoms, dienyl comprising from 3 to 20 carbon atoms, allyl comprising from 3 to 20 carbon atoms, ethynyl comprising from 2 to 20 carbon atoms, substituted or non-substituted, F_1 preferably corresponding to the following formula:

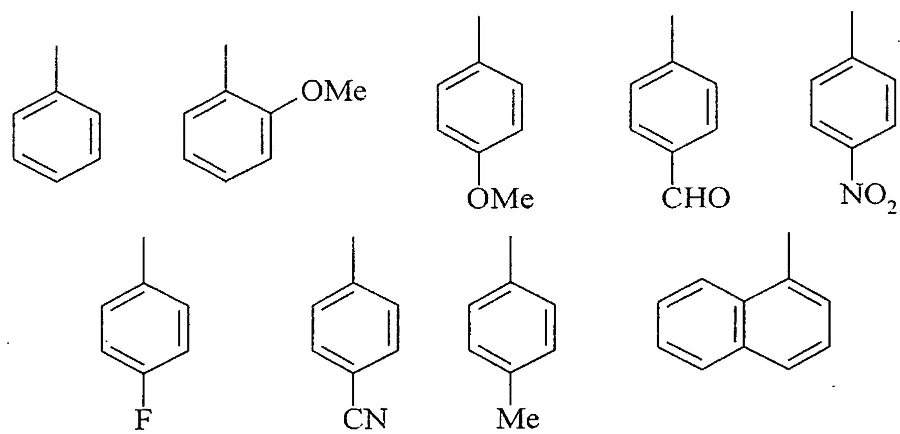


Ar_2 corresponding to an aryl group, substituted or non-substituted, comprising from 6 to 30 carbon atoms,

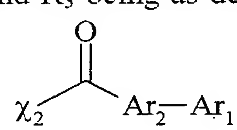
– F_2 is in the form $-R_q-R_e$, R_q and R_e being as defined above, F_2 preferably corresponding to the following formula:



Ar_1 representing an aromatic group preferably chosen from:

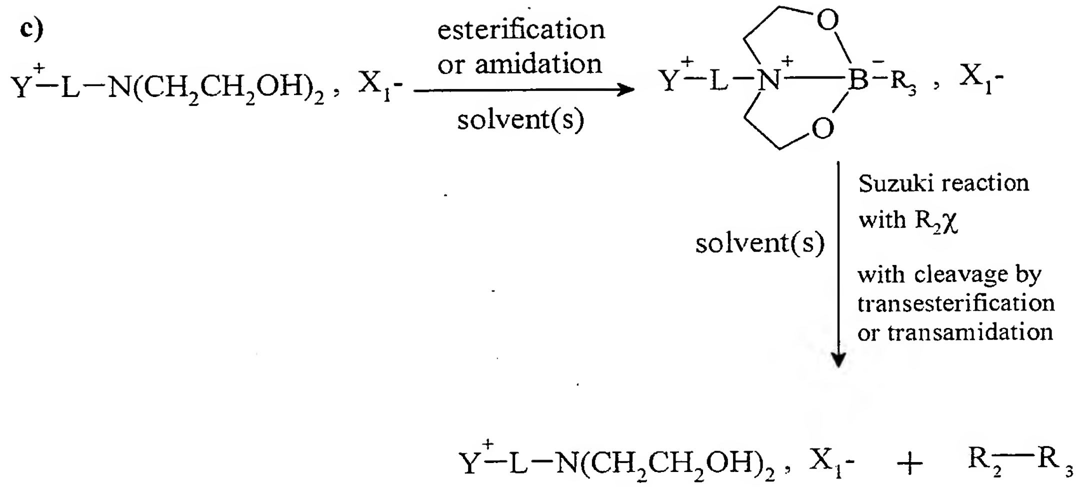


the molecule G being in the form R_2-R_3, R_2 and R_3 being as defined above, and corresponding in particular to the following formula:



in which χ_2, Ar_1 and Ar_2 are as defined above,

c)



Y^+–, L, X_1^-, R_2 and R_3 being as defined above,

R_3 preferably being a phenyl group,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents.

Embodiment a) corresponds to the case where the aryl halide is supported and where the boronic acid is free.

Embodiment b) corresponds to the case where the boronic acid is supported and where the aryl halide is free.

Embodiments a), b) and c) make it possible to easily purify the coupling products in the form of salts. In particular, it is easy to eliminate the homocoupling products which are not salts by simple washing before transesterification.

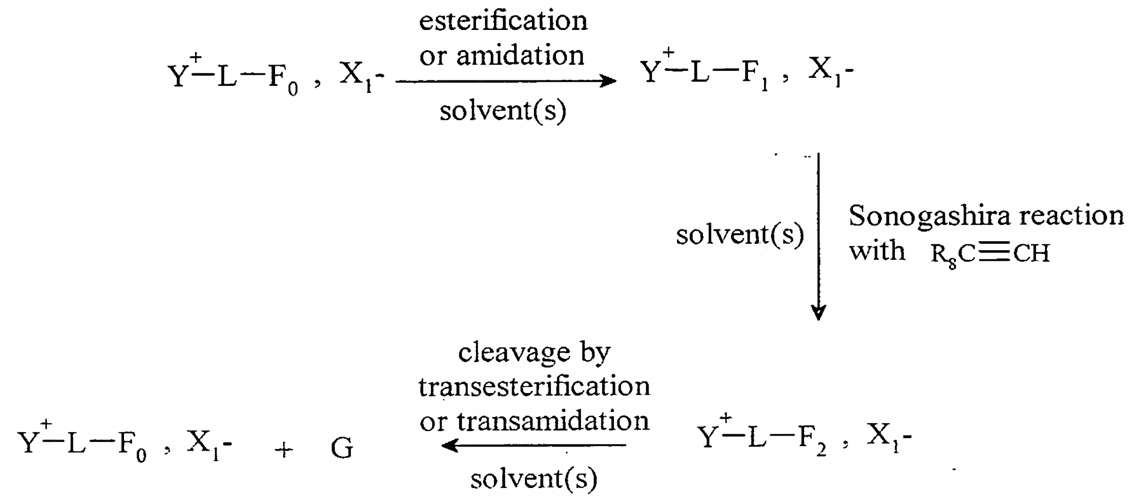
The advantages of these different embodiments are the following:

– reactions on soluble support lend themselves to the techniques of combinatorial chemistry and parallel synthesis;

– these supports are easy to purify as they are salts which are insoluble in a certain number of solvents; they can therefore be washed and/or recrystallized; in particular, in the case of the Suzuki reaction, the homocoupling product can be easily eliminated by simple washing of the salt before transesterification.

The present invention also relates to the use as defined above, for the implementation of Sonogashira coupling, according to one of the following reaction diagrams:

a)



$Y^+\!-$ representing an onium cation as defined above, and preferably being a trimethylalkylammonium, triethylalkylammonium, tributylalkylphosphonium, N-methylimidazolium or pyridinium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group, comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 1 to 10,

X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

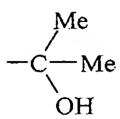
R_8 representing an OR_h, NR_hR_u, COR_h, CN, SO_2R_h, SR_h group, an alkenyl, ethynyl, dienyl group, R_h and R_u representing, independently of one another, a hydrogen atom, an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms,

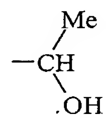
or R_8 representing an alkyl group, branched or linear, optionally functional, comprising from 1 to 20 carbon atoms, or an aryl group, or an alkaryl or aralkyl group, comprising from 6 to 30 carbon atoms, substituted or non-substituted, said alkyl or aryl groups being able to be substituted by one of the following functional groups: a halogen atom, in particular Cl, an OR_h, NR_hR_u, COR_h, CN, SO_2R_h, SR_h group, an alkenyl, ethynyl, dienyl, vinyl, alkynyl group, R_h and R_u being as defined previously,

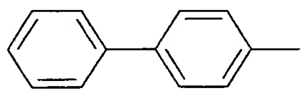
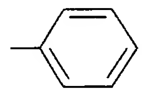
R_8 being in particular one of the following groups:

$-(CH_2)_s-CH_3$, $-(CH_2)_s-CH_2OH$, $-(CH_2)_s-CH_2OMe$,

s representing an integer comprised between 0 and 10,



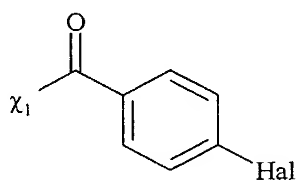




Me_3Si-

the functions F_0, F_1 and F_2 being as defined below:

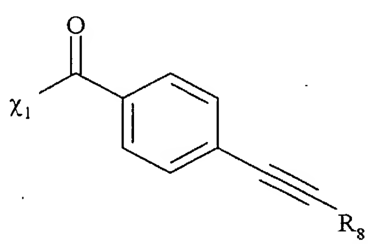
– F_0 corresponds to a $-\chi_1H$ group, in which χ_1 represents an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

– F_1 corresponds to the following formula:



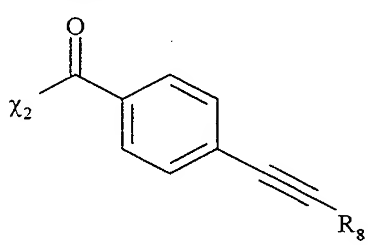
χ_1 being as defined above, and Hal representing a halogen, and preferably being iodine,

– F_2 corresponds to the following formula:



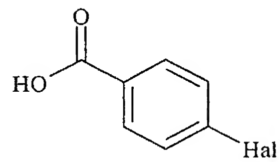
χ_1 and R_8 being as defined above,

G corresponding to the following formula:

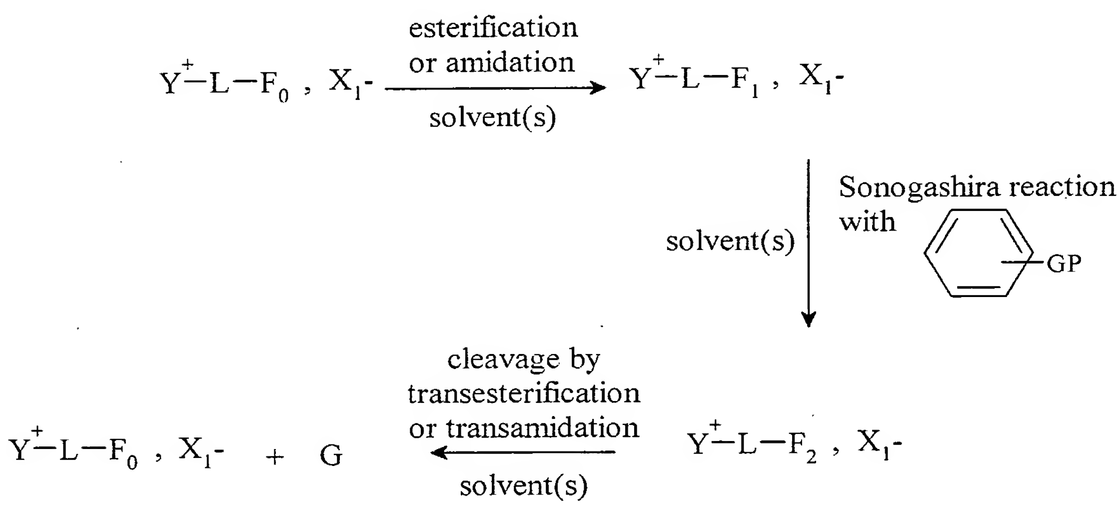


in which χ_2 represents either an $-OR_g$ group, R_g representing a hydrogen atom or an alkyl group comprising from 1 to 20 carbon atoms, or an $-NR_hR_u$ group, R_h and R_u representing independently of one another a hydrogen atom, an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms, χ_2 representing in particular an OMe, OEt, OPr or OBu group.

The conversion of the function F_0 to F_1 is carried out by an esterification or amidation reaction with the carboxylic acid of formula:



b)



Y^+– representing an onium cation as defined above, and preferably being a trimethylalkylammonium, triethylalkylammonium, tributylalkylphosphonium, N-methylimidazolium, alkylpyridinium, dimethylalkylsulphonium or diethylalkyl-sulphonium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group, comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 1 to 10,

X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

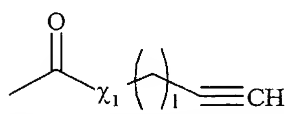
the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

GP representing a leaving group, and being in particular Cl, Br, I or OTf,

the functions F_0, F_1 and F_2 being as defined below:

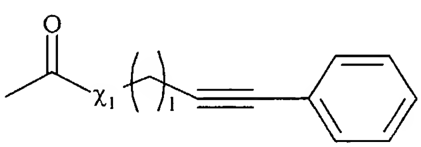
– F_0 corresponds to a -COOH group,

– F_1 corresponds to the following formula:



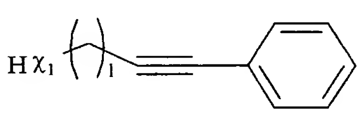
in which l represents an integer varying from 1 to 20, and χ_1 represents an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

– F_2 corresponds to the following formula:



χ_1 and l being as defined above,

G corresponding to the following formula:



in which χ_1 and l are as defined above.

Embodiment a) corresponds to the case where the aromatic is supported and where the acetylenic is free.

Embodiment b) corresponds to the case where the acetylenic is supported and where the aromatic is free.

The present invention also relates to the use as defined above, for the implementation of the Baylis-Hilman reaction, according to one of the following reaction diagrams:

a)

$$\overset{+}{Y}-L-F_0\ ,\ X_1^- \xrightarrow[\text{solvent(s)}]{\text{esterification or amidation}} \overset{+}{Y}-L-F_1\ ,\ X_1^-$$

$$\overset{+}{Y}-L-F_1\ ,\ X_1^- \xrightarrow[\text{solvent(s)}]{\text{Baylis-Hilman reaction with ArCHO}} \overset{+}{Y}-L-F_2\ ,\ X_1^-$$

$$\overset{+}{Y}-L-F_0\ ,\ X_1^- \ +\ G \xleftarrow[\text{solvent(s)}]{\text{cleavage by transesterification or transamidation}} \overset{+}{Y}-L-F_2\ ,\ X_1^-$$

Y^+- representing an onium cation as defined above, and preferably being a trimethylalkylammonium, triethylalkylammonium, tributylalkylphosphonium, N-methylimidazolium or pyridinium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group, comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 1 to 10,

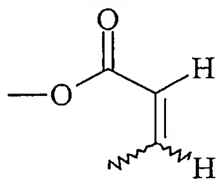
X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

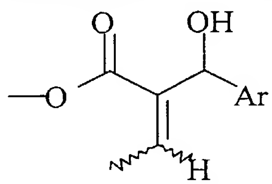
the functions F_0, F_1 and F_2 being as defined below:

– F_0 represents an -OH group,

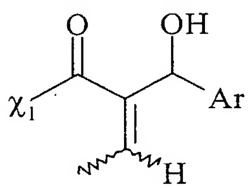
– F_1 corresponds to the following formula:



– F_2 corresponds to the following formula:



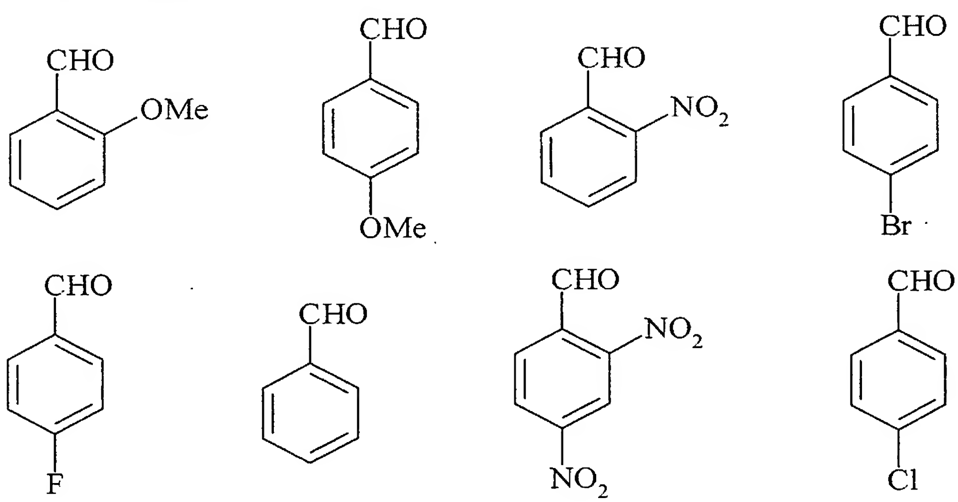
G corresponding to the following formula:



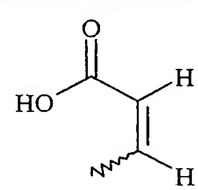
χ_1 representing an -OH group, or an -OR_g group, R_g representing a linear or branched alkyl group, comprising from 1 to 20 carbon atoms,

Ar representing an aromatic or heteroaromatic group, substituted or non-substituted,

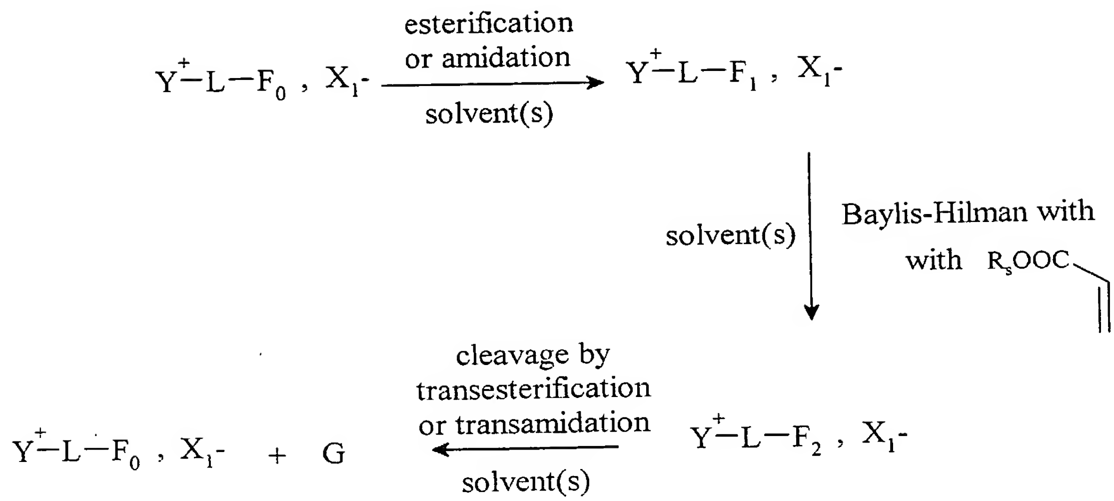
ArCHO being in particular chosen from:



The conversion of the function F_0 to F_1 is carried out by an esterification or amidation reaction with the carboxylic acid of formula:



b)



Y^+- representing an onium cation as defined above, and preferably being a trimethylalkylammonium, triethylalkylammonium, tributylalkylphosphonium, N-methylimidazolium, alkylpyridinium, dimethylalkylsulphonium or diethylalkyl-sulphonium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group, comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 1 to 10,

X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

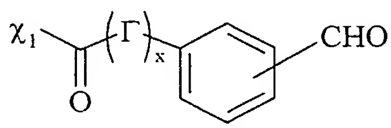
the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

R_s representing a hydrogen atom or an alkyl group comprising from 1 to 20 carbon atoms or aralkyl or alkaryl comprising from 7 to 30 carbon atoms,

the functions F_0, F_1 and F_2 being as defined below:

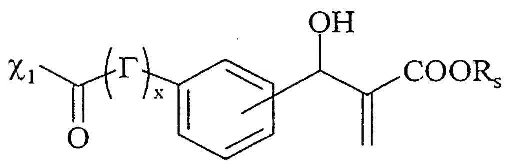
– F_0 corresponds to a $-\chi_1H$ group, in which χ_1 represents an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

– F_1 corresponds to the following formula:



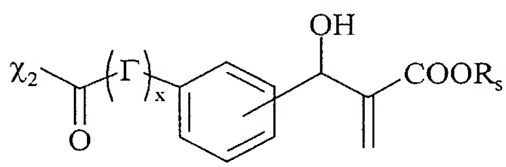
χ_1 being as defined above,
x being equal to 0 or 1,
Γ representing an alkyl chain comprising from 1 to 20 carbon atoms, alkaryl, aralkyl comprising from 6 to 30 carbon atoms,

– F_2 corresponds to the following formula:



χ_1, x, R_s and Γ being as defined above

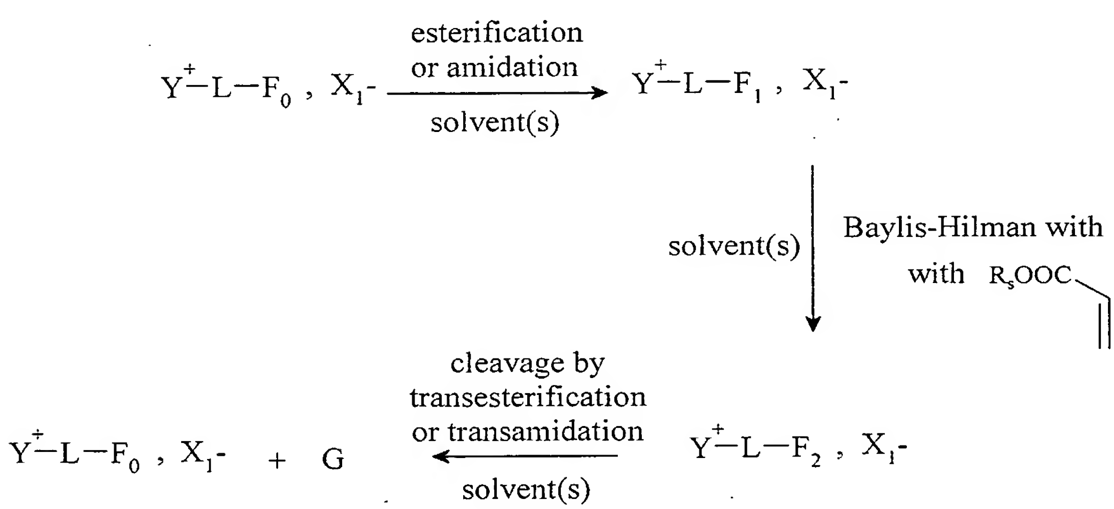
– G corresponding to the following formula:



χ_2, x, R_s and Γ being as defined above

in which χ_2 represents either an $-OR_g$ group, R_g representing a hydrogen atom or an alkyl group comprising from 1 to 20 carbon atoms, or an $-NR_hR_u$ group, R_h and R_u representing independently of one another a hydrogen atom, an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms, χ_2 representing in particular an OMe, OEt, OPr or OBu group.

c)



Y^{+}– representing an onium cation as defined above, and preferably being a trimethylalkylammonium, triethylalkylammonium, tributylalkylphosphonium, N-methylimidazolium or pyridinium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group, comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 1 to 10,

X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

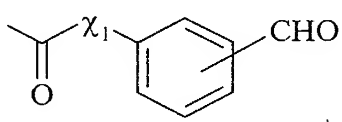
the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

R_s representing a hydrogen atom or an alkyl group comprising from 1 to 20 carbon atoms or aralkyl or alkaryl comprising from 7 to 30 carbon atoms,

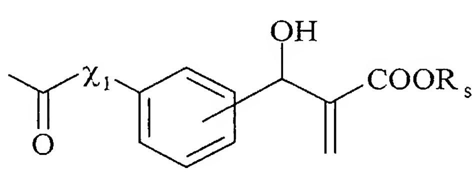
the functions F_0, F_1 and F_2 being as defined below:

– F_0 corresponds to a $-CO\chi_1H$ group, in which χ_1 represents an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

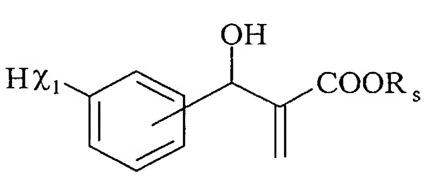
– F_1 corresponds to the following formula:



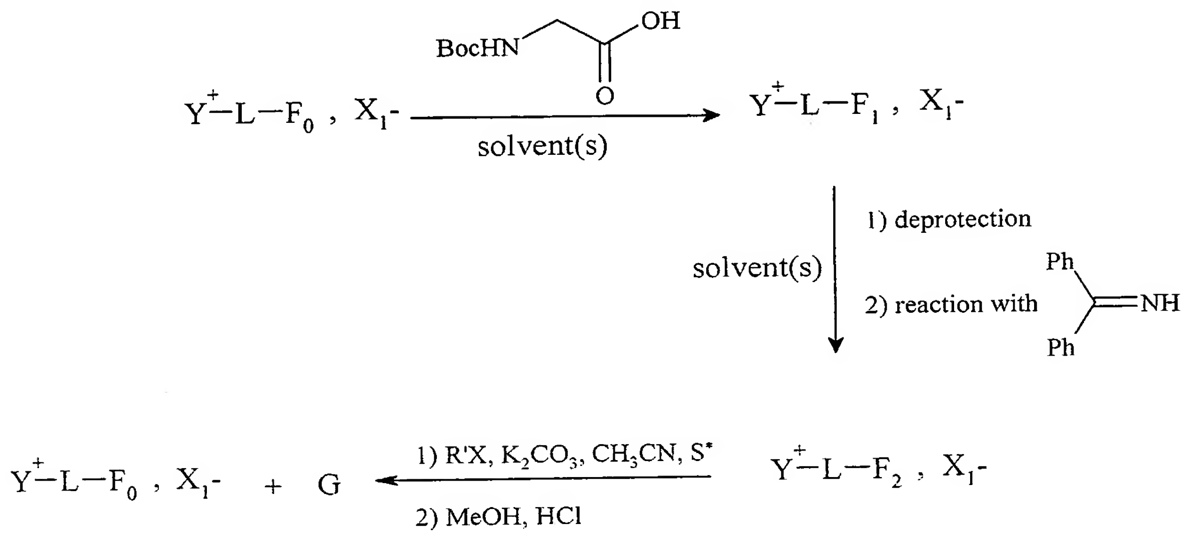
– F_2 corresponds to the following formula:



– G corresponding to the following formula:



The present invention also relates to the use as defined above, for the synthesis, optionally asymmetrical, of α-amino acids, according to the following reaction diagram:



Y^+– representing an onium cation as defined above, and preferably being a trimethylalkylammonium, triethylalkylammonium or tributylalkylphosphonium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl group comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 3 to 6,

X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $^-N(SO_2CF_3)_2$, BF_4^-, PF_6^-,

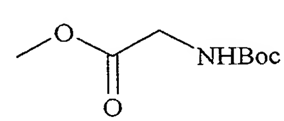
the solvent or solvents being chosen from: acetonitrile, dichloromethane, tetrahydrofuran, dioxane, toluene, chlorobenzene or a mixture of these solvents,

R' representing a linear or branched alkyl group, comprising from 1 to 30 carbon atoms, optionally functional,

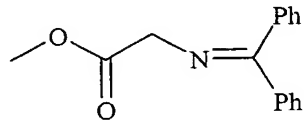
S^* representing a chiral phase transfer agent such as O(9)-allyl-N-9-anthracenyl-methylcinchonidinium bromide (see Corey et al., 1998),

the functions F_0, F_1 and F_2 being as defined below:

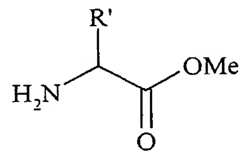
- F_0 corresponds to -OH,
- F_1 corresponds to the following formula:



– F_2 corresponds to the following formula:



G corresponding to the following formula:



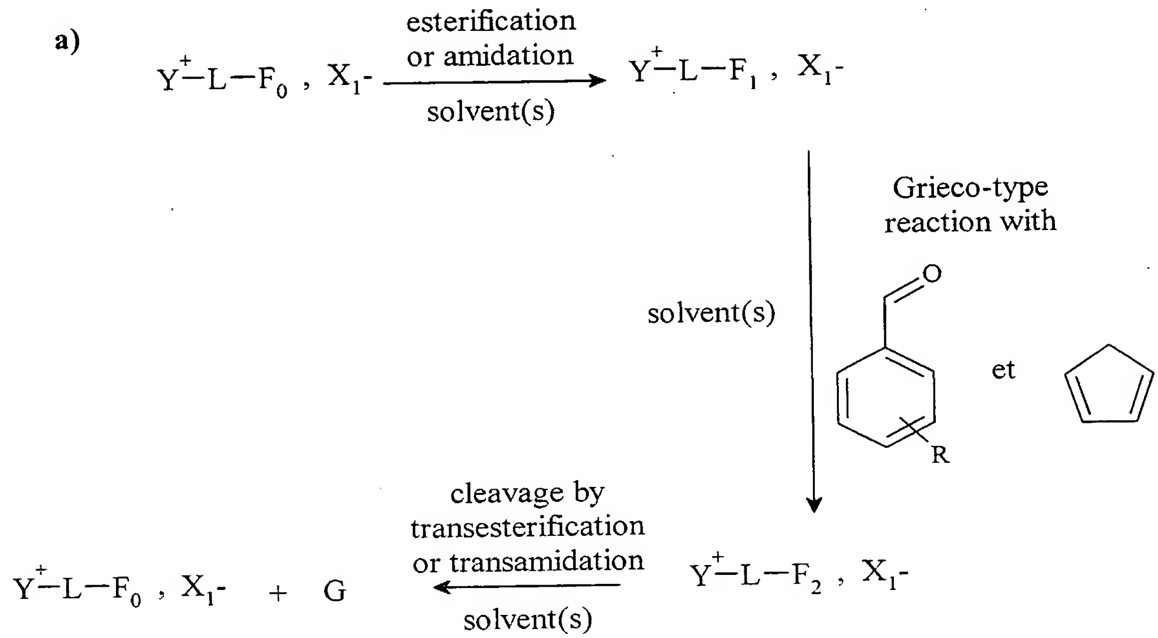
The present invention also relates to the use as defined above, for the implementation of multi-component reactions.

Multi-component reactions (MCRs) simultaneously bring together at least three partners under experimental conditions which do not vary over time and allow the creation of several covalent bonds in cascade in a single reactor, unlike standard reactions where two reagents lead to a product by the creation of a new bond. Thus it is possible in a single stage to access a highly functionalized molecule from relatively simple entities. Moreover the MCRs combine convergence and economy of atoms, two essential principles in organic synthesis and also in combinatorial chemistry. Finally, these reactions generally take place with a high yield, since they avoid the succession of stages of linear or multi-stage syntheses which, at each step, cause a drop in yield.

The best-known and most highly developed MCRs are those of Passerini and Ugi (Ugi et al., 1999; Ugi et al., 2001; Domling et al., 2000; Ugi, 2001; Bienayme et al., 2000; Vanden Eynde et al., 2000; Domling, 2002).

The present invention also relates to the use as defined above, for the implementation of UGI-type multi-component reactions, in particular for the Grieco-type reaction according to one of the following reaction diagrams:

a)



Y^+– representing an onium cation as defined above, and preferably being a trimethylalkylammonium, triethylalkylammonium, tributylalkylphosphonium, N-methyl-N'-alkylimidazolium, N-alkylpyridinium, dimethylalkylsulphonium or diethylalkylsulphonium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group, comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 1 to 10,

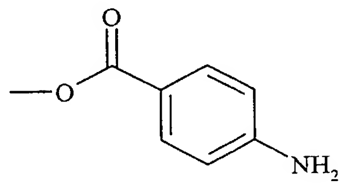
X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

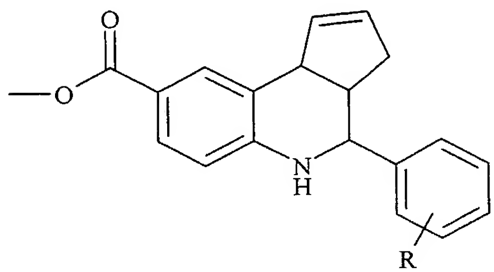
R representing a hydrogen atom, a nitro group, preferably in para position, a chlorine atom, preferably in para position or a methoxy group, preferably in para position,

the functions F_0, F_1 and F_2 being as defined below:

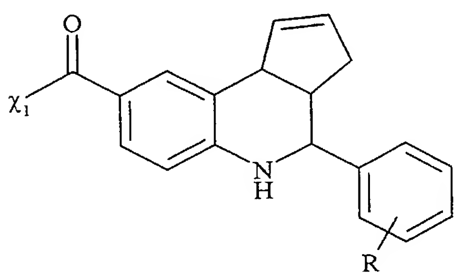
- F_0 represents an -OH group,
- F_1 corresponds to the following formula:



- F_2 corresponds to the following formula:

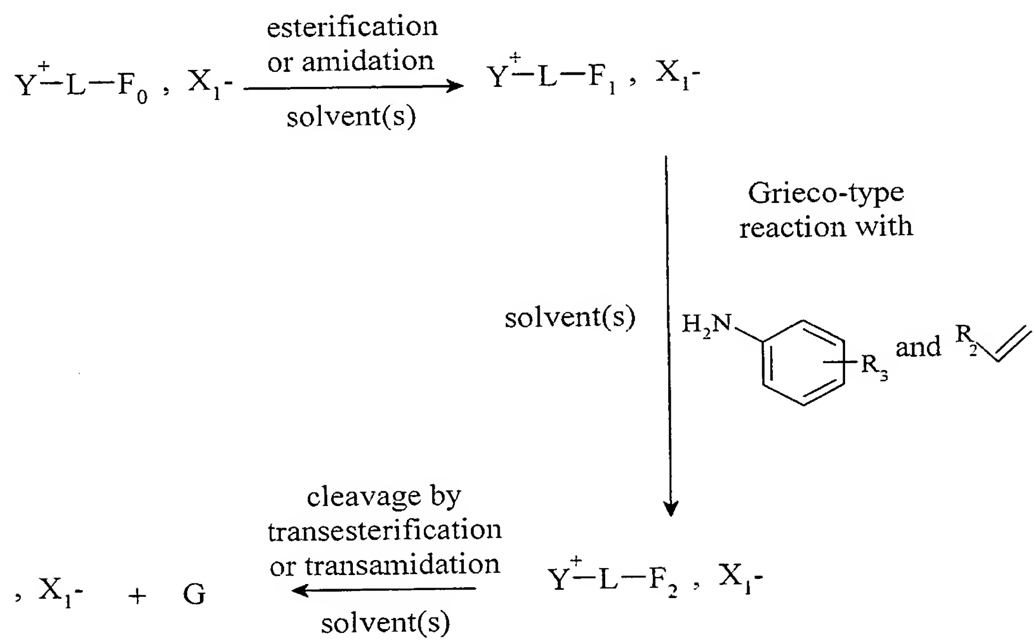


G corresponding to the following formula:



χ_1 representing an -OH group, or an $-OR_g$ group, R_g representing a linear or branched alkyl group, comprising from 1 to 20 carbon atoms,

b)



Y^+– representing an onium cation as defined above, and preferably being a trimethylalkylammonium, triethylalkylammonium, tributylalkylphosphonium, N-methyl-N'-alkylimidazolium, N-alkylpyridinium, dimethylalkylsulphonium or diethylalkylsulphonium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group, comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 1 to 10,

X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

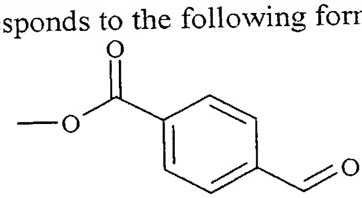
R_2 representing a functional or non-functional alkyl group, comprising from 1 to 20 carbon atoms, or a functional or non-functional aryl group, comprising from 6 to 30 carbon atoms, or an aralkyl or alkaryl group, functional or non-functional, comprising from 7 to 50 carbon atoms,

R_3 representing a hydrogen atom, a linear or branched alkyl group, comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms, or an aralkyl or alkaryl group, functional or non-functional, comprising from 7 to 50 carbon atoms, or a functional group in particular chosen from NO_2, CN, COOR, OR, COR, NHCOR, NRR', SO_2R, I, Br, R and R' representing independently of one another an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms,

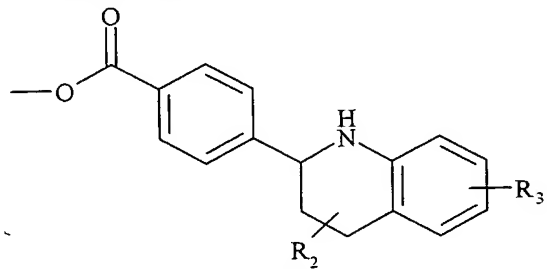
the functions F_0, F_1 and F_2 being as defined below:

– F_0 represents an -OH group,

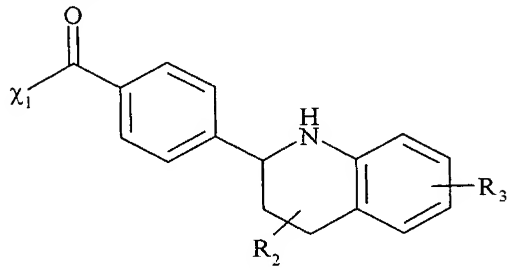
– F_1 corresponds to the following formula:



– F_2 corresponds to the following formula:

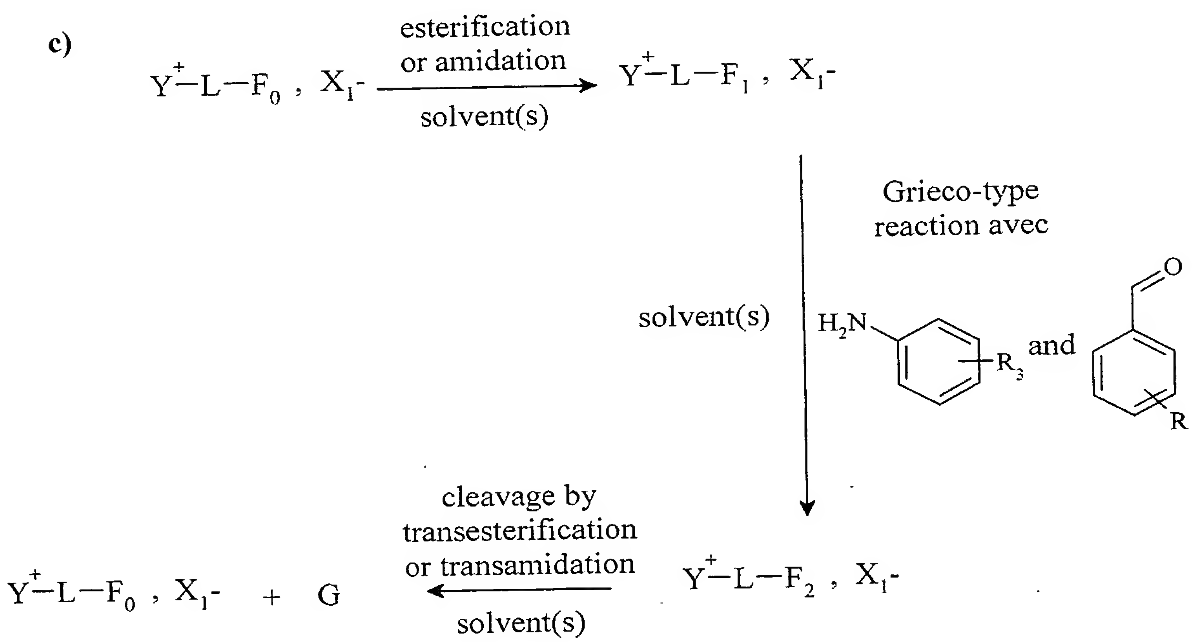


G corresponding to the following formula:



χ_1 representing an -OH group, or an -OR$_g$ group, R_g representing a linear or branched alkyl group, comprising from 1 to 20 carbon atoms.

c)



Y^+– representing an onium cation as defined above, and preferably being a trimethylalkylammonium, triethylalkylammonium, tributylalkylphosphonium, N-methyl-N'-alkylimidazolium, N-alkylpyridinium, dimethylalkylsulphonium or diethylalkylsulphonium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group,

comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 1 to 10,

X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

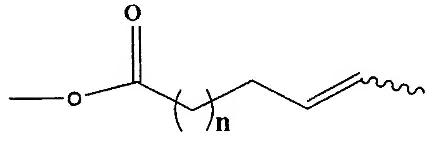
R representing a hydrogen atom or a functional group such as a nitro group in para position, a chlorine atom in para position or a methoxy group in ortho position, or a functional or non-functional alkyl group, comprising from 1 to 20 carbon atoms, or a functional or non-functional aryl group, comprising from 6 to 30 carbon atoms, or an aralkyl or alkaryl group, functional or non-functional, comprising from 7 to 50 carbon atoms,

R_3 representing a hydrogen atom, a linear or branched alkyl group, comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms, or an aralkyl or alkaryl group, functional or non-functional, comprising from 7 to 50 carbon atoms, or a functional group in particular chosen from NO_2, CN, COOR, OR, COR, NHCOR, NRR', SO_2R, I, Br, R and R' representing independently of one another an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms,

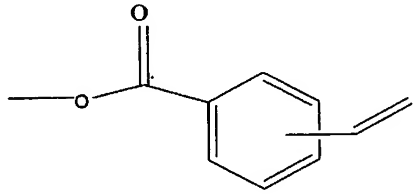
the functions F_0, F_1 and F_2 being as defined below:

– F_0 represents any function making it possible to attach and release a radical carrying an olefin, preferably an ester, or an amide.

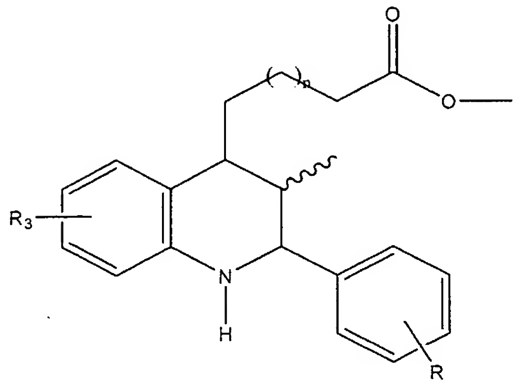
– F_1 corresponds to one of the following general formulae:



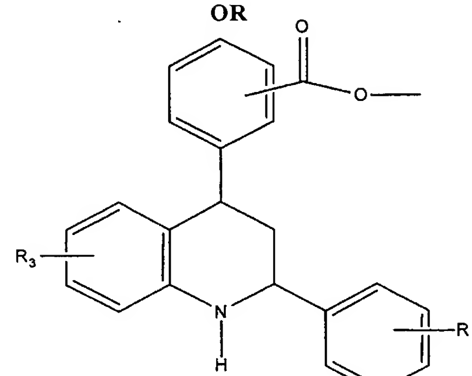
n representing an integer varying from 1 to 10



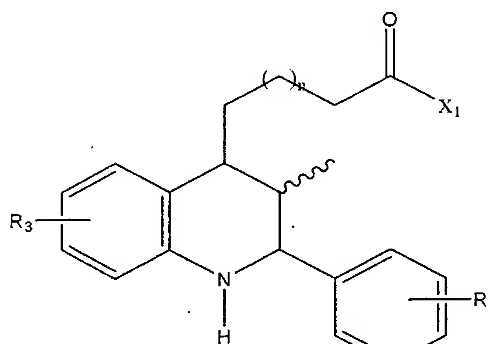
– F_2 corresponds to one of the following general formulae:



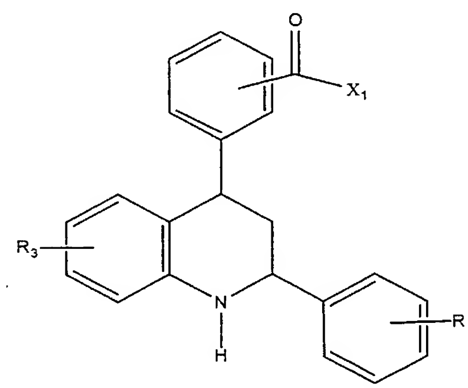
OR



G corresponding to one of the following general formulae:



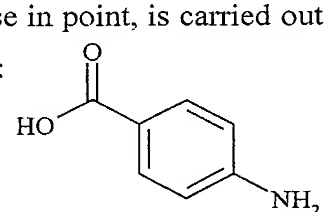
OR



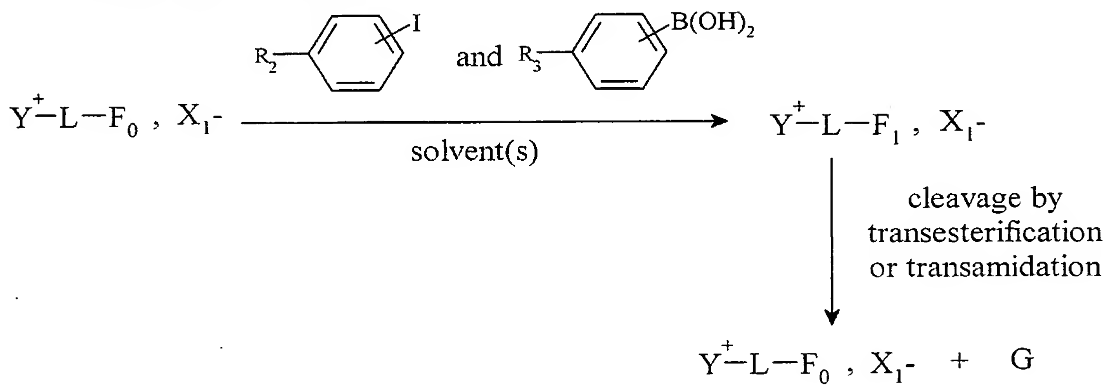
n, R and R_3 being as defined above, and

χ_1 representing an -OH group, or an -OR_g group, R_g representing a linear or branched alkyl group, comprising from 1 to 20 carbon atoms.

The conversion of the function F_0 to F_1, in the first case in point, is carried out by an esterification reaction with the carboxylic acid of formula:



The present invention also relates to the use as defined above, for the implementation of multi-component reactions, in particular for the synthesis of tetrasubstituted olefins according to R.C. Larock et al. (2003), according to the following reaction diagram:



Y^+– representing an onium cation as defined above, and preferably being a trimethylalkylammonium, triethylalkylammonium, tributylalkylphosphonium, N-methyl-N'-alkylimidazolium, N-alkylpyridinium, dimethylalkylsulphonium or diethylalkylsulphonium cation,

L representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group, comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 1 to 10,

X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

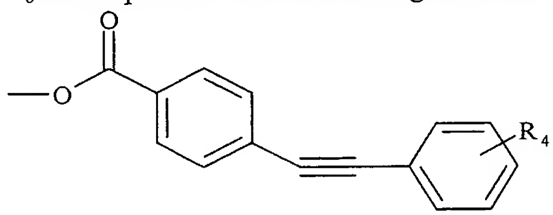
the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

R_2 and R_3, preferably in para position, representing a hydrogen atom, a linear or branched, optionally functional alkyl group comprising from 1 to 30 carbon atoms, an optionally substituted and/or functional aryl group, comprising from 6 to 30 carbon

atoms, a functional group, preferably a methoxy, mono-alkylamino, dialkylamino, arylamino, cyano, ester, nitro, ketone, sulphonyl, alkylthio, sulphoxide group,

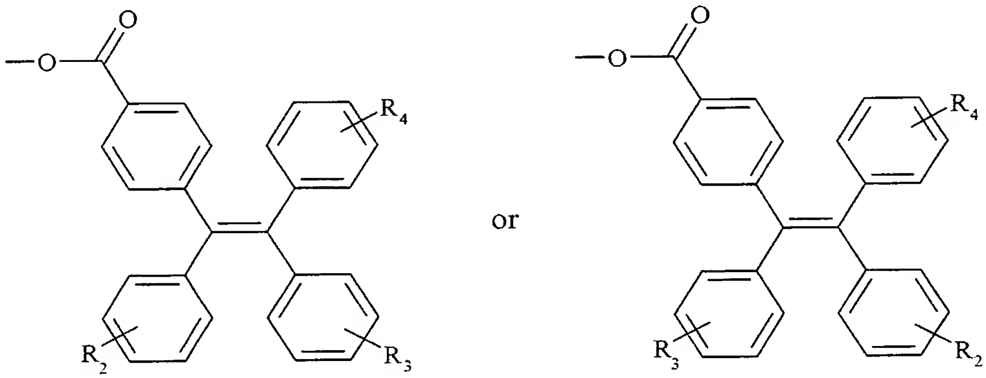
the functions F_0 and F_1 being as defined below:

– F_0 corresponds to the following formula:



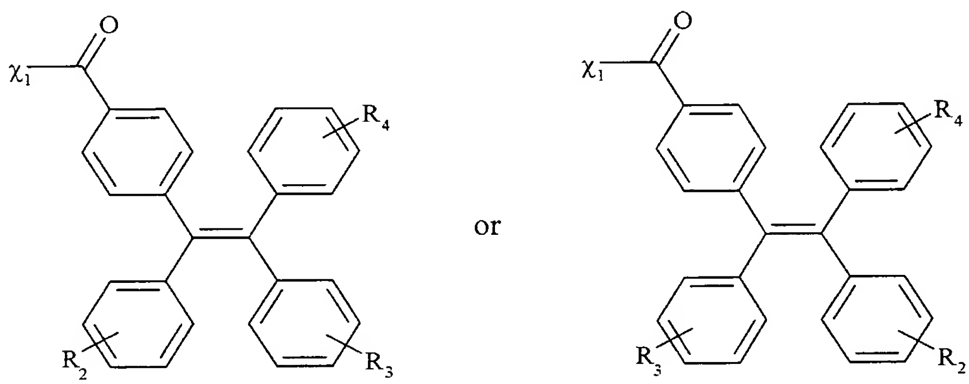
R_4 representing a group as defined for R_2 and R_3 above,

– F_1 corresponds to one of the following formulae:



R_2, R_3 and R_4 being as defined above,

G corresponds to one of the following formulae:

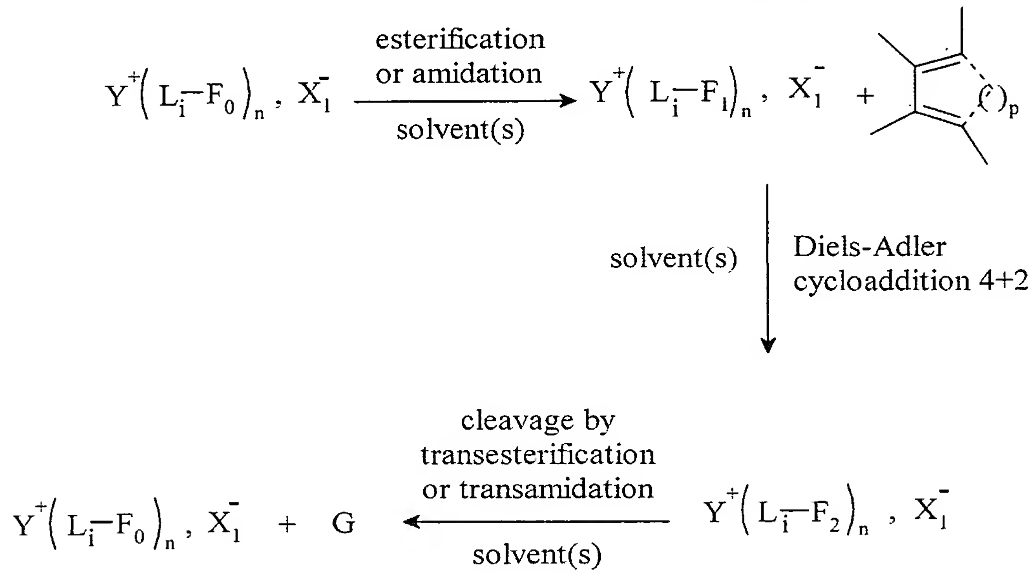


χ_1 representing an -OH group, or an -OR$_g$ group, R_g representing a linear or branched alkyl group, comprising from 1 to 20 carbon atoms.

The conversion of F_0 to F_1 is carried out by a cis-addition of the aryl group originating from the aryl halide of the least hindered side to the end of the starting alkyne which is richest in electrons, whilst the acyl group originating from the arylboronic acid is added to the other end.

Within the scope of the present invention, it is also possible to use polyfunctional cations, which are defined as being cations carrying several functions, said functions being identical or different.

The present invention also relates to the use as defined above, for the implementation of cycloaddition reactions, preferably for the implementation of the Diels-Alder reaction, according to the following reaction diagram:



n being an integer varying from 2 to 4, as defined below,

i being an integer varying from 1 to n,

p being an integer varying from 0 to 2,

Y^+ representing an onium cation as defined above, of formula $(R_b)_{x-n}A^+$ in which x represents an integer equal to 3 or 4, n being equal to 2, 3 or 4 when x is equal to 4 and n being equal to 2 or 3 when x is equal to 3, R_b represents an alkyl group comprising from 1 to 20 carbon atoms, an aryl group comprising from 6 to 30 carbon atoms or an aralkyl or alkaryl group comprising from 6 to 30 carbon atoms, said abovementioned alkyl, aryl, aralkyl or alkaryl groups being non-functional, and in which A^+ represents an ammonium, imidazolium, phosphonium or sulphonium cation, Y^+ representing in particular an alkylammonium, alkylphosphonium or alkylsulphonium cation, and preferably being a tetraalkylammonium, tetraalkylphosphonium, dialkylimidazolium, trialkylsulphonium cation,

L_i representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group,

comprising from 6 to 30 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 2 to 10, the arms L_i being able to be identical or different,

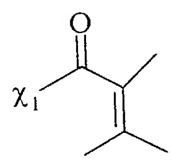
X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

the functions F_0, F_1 and F_2 being as defined below:

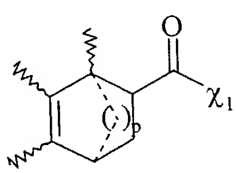
– F_0 corresponds to a $-\chi_1H$ group, in which χ_1 represents an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

– F_1 corresponds to the following formula:



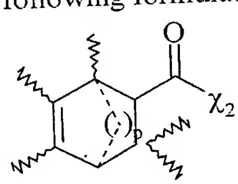
χ_1 being as defined above,

– F_2 corresponds to the following formula:



χ_1 being as defined above,

G corresponding to the following formula:

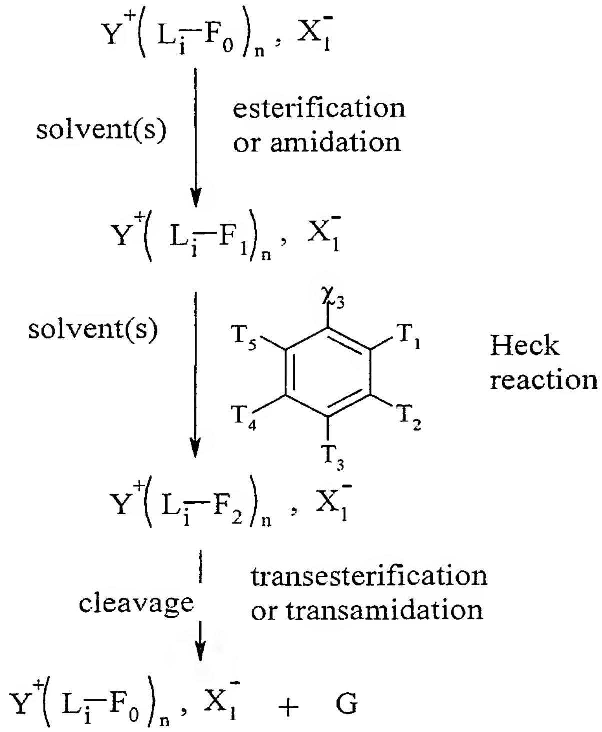


in which χ_2 represents either an OR_g group, R_g representing a hydrogen atom or an alkyl group comprising from 1 to 20 carbon atoms, or an $-NR_hR_u$ group, R_h and R_u representing independently of one another a hydrogen atom, an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms.

The notation $Y^+(L_i\text{-}F_0)_n$ means that the entity Y^+ is substituted by n $L_i\text{-}F_0$ entities linked by a covalent bond.

The use of a plurifunctional salt within the framework of the Diels-Alder reaction makes it possible to increase the productivity of the solutions used. Moreover, the arm can be functionalized differently and allow either intramolecular reactions, or cascade reactions, or multicomponent reactions.

The present invention relates to the use as defined above, for the implementation of the Heck reaction, according to the following reaction diagram:



n being an integer varying from 2 to 4, as defined below,

i being an integer varying from 1 to n,

Y^+ representing an onium cation as defined above, of formula $(R_b)_{x-n}\Lambda^+$ in which x represents an integer equal to 3 or 4, n being equal to 2, 3 or 4 when x is equal to 4 and n being equal to 2 or 3 when x is equal to 3, R_b represents an alkyl group comprising from 1 to 20 carbon atoms, an aryl group comprising from 6 to 30 carbon atoms or an aralkyl or alkaryl group comprising from 6 to 30 carbon atoms, said abovementioned alkyl, aryl, aralkyl or alkaryl groups being non-functional, and in which Λ^+ represents an ammonium, imidazolium, phosphonium or sulphonium cation, Y^+ representing in particular an alkylammonium, alkylphosphonium or alkylsulphonium

cation, and preferably being a tetraalkylammonium, tetraalkylphosphonium, dialkylimidazolium, trialkylsulphonium cation,

L_i representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group, comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 2 to 10, the arm L_i being able to be identical or different,

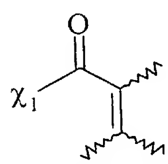
X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

the functions F_0, F_1 and F_2 being as defined below:

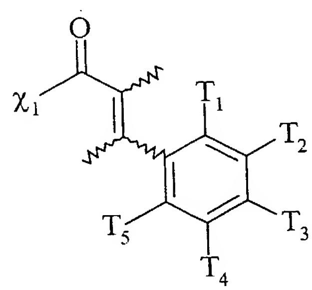
– F_0 corresponds to a $-\chi_1H$ group, in which χ_1 represents an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

– F_1 corresponds to the following formula:



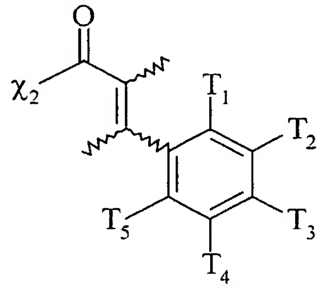
χ_1 being as defined above,

– F_2 corresponds to the following formula:



χ_1 being as defined above,

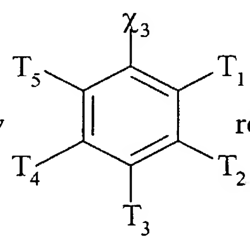
G corresponding to the following formula:

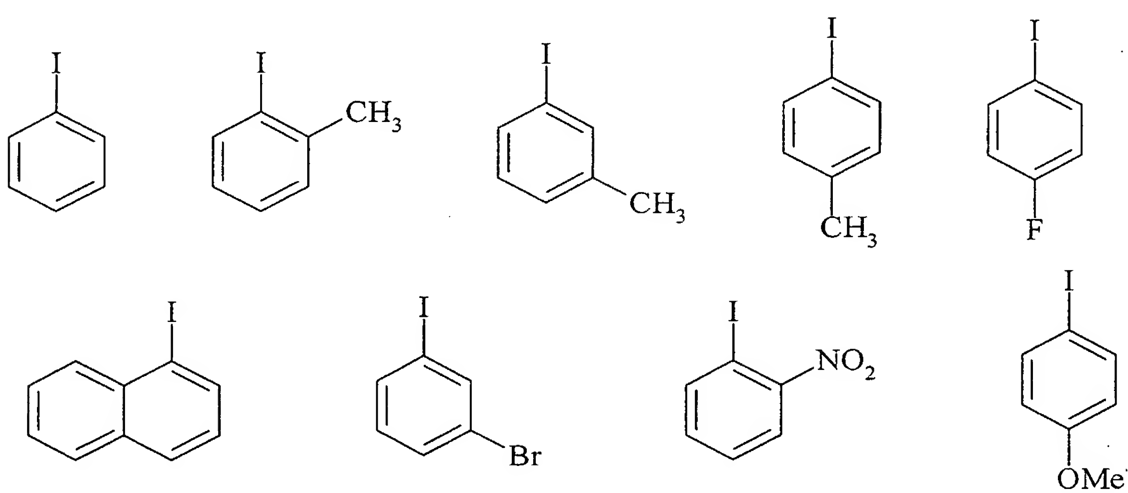


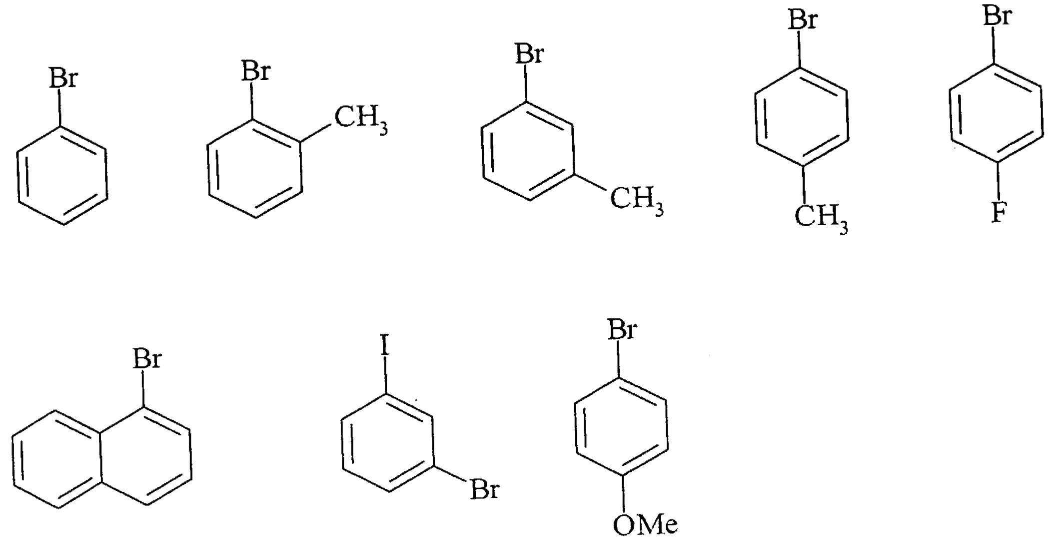
in which χ_2 represents either an $-OR_g$ group, R_g representing a hydrogen atom or an alkyl group comprising from 1 to 20 carbon atoms, or an $-NR_hR_u$ group, R_h and R_u representing independently of one another a hydrogen atom, an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms,

χ_3 representing a leaving group, in particular chosen from the I, Cl and Br halides, the mesylate, tosylate, triflate, sulphonate, sulphate or phosphate groups,

T_1, T_2, T_3, T_4 and T_5 representing independently of one another a hydrogen atom, a linear or branched alkyl group, comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms, or a functional group in particular chosen from NO_2, CN, COOR, OR, COR, NHCOR, NRR'', SO_2R, I, Br, R and R'' representing independently of one another an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms,

the entity  representing in particular the following groups:





The use of a plurifunctional salt within the framework of the Heck reaction makes it possible to increase the productivity of the solutions used. Moreover, the arm can be functionalized differently and allow either intramolecular reactions, or cascade reactions or multicomponent reactions.

The present invention also relates to the use as defined above, for the implementation of Suzuki coupling, according to the following reaction diagram:

$$Y^{+}\left(L_{i}-F_{0}\right)_{n}, X_{1}^{-} \xrightarrow[\text{solvent(s)}]{\text{esterification or amidation}} Y^{+}\left(L_{i}-F_{1}\right)_{n}, X_{1}^{-}$$

$$Y^{+}\left(L_{i}-F_{1}\right)_{n}, X_{1}^{-} \xrightarrow[\text{solvent(s)}]{\text{Suzuki reaction with } R_3B(OR_7)_2} Y^{+}\left(L_{i}-F_{2}\right)_{n}, X_{1}^{-}$$

$$Y^{+}\left(L_{i}-F_{0}\right)_{n}, X_{1}^{-} + G \xleftarrow[\text{solvent(s)}]{\text{cleavage by transesterification or transamidation}} Y^{+}\left(L_{i}-F_{2}\right)_{n}, X_{1}^{-}$$

R_3 being chosen from the substituted or non-substituted aryl, heteroaryl, ethenyl, dienyl, allyl, ethynyl groups, comprising from 2 to 30 carbon atoms,

R_7 representing a hydrogen atom or a branched or linear alkyl group, or a cycloalkyl group comprising from 1 to 12 carbon atoms,

n being an integer varying from 2 to 4, as defined below,

i being an integer varying from 1 to n,

Y^+ representing an onium cation as defined above, of formula $(R_b)_{x-n}\Lambda^+$ in which x represents an integer equal to 3 or 4, n being equal to 2, 3 or 4 when x is equal to 4 and n being equal to 2 or 3 when x is equal to 3, R_b represents an alkyl group comprising from 1 to 20 carbon atoms, an aryl group comprising from 6 to 30 carbon atoms or an aralkyl or alkaryl group comprising from 6 to 30 carbon atoms, said abovementioned alkyl, aryl, aralkyl or alkaryl groups being non-functional, and in which Λ^+ represents an ammonium, imidazolium, phosphonium or sulphonium cation, Y^+ representing in particular an alkylammonium, alkylphosphonium or alkylsulphonium cation, and preferably being a tetraalkylammonium, tetraalkylphosphonium, dialkylimidazolium, trialkylsulphonium cation,

L_i representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group, comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 2 to 10, the arms L_i being able to be identical or different,

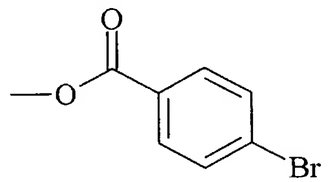
X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

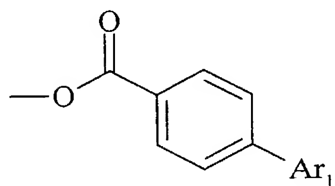
the functions F_0, F_1 and F_2 being as defined below:

– F_0 is in the form $-\chi_1H$, χ_1 representing an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

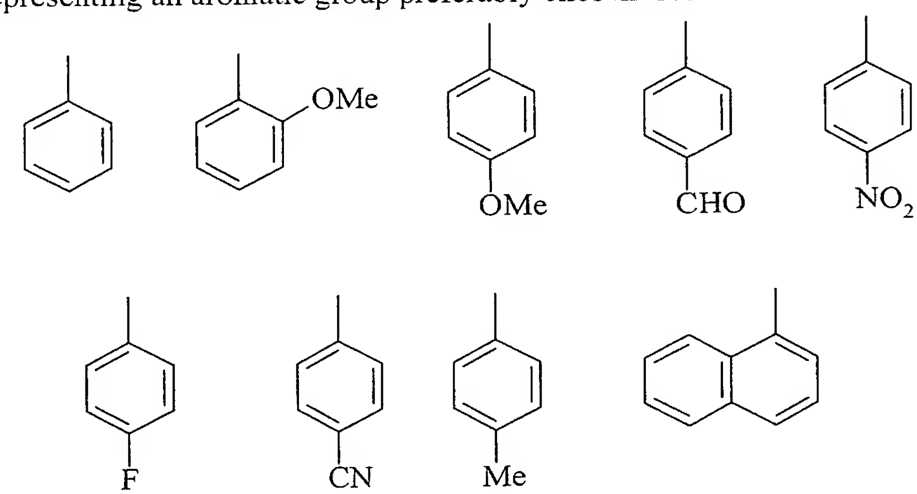
– F_1 is in the form $-R_e-\chi$, R_e representing an aromatic or heteroaromatic group comprising from 6 to 30 carbon atoms, χ representing a leaving group preferably chosen from Cl, Br, I, OTf, $O\text{-}CO_2R^5$ or $OSO_3\text{-}R^5$, R^5 representing an alkyl group comprising from 1 to 10 carbon atoms or an aralkyl group comprising from 6 to 30 carbon atoms, F_1 preferably corresponding to the following formula:



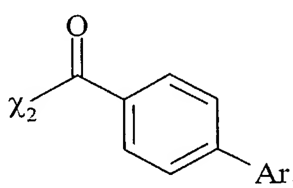
– F_2 is in the form $-R_e-R_2$, R_e being as defined above and R_2 being chosen from the aryl, heteroaryl, ethenyl, dienyl, allyl, ethynyl groups, substituted or non-substituted, comprising from 2 to 30 carbon atoms, F_2 preferably corresponding to the following formula:



Ar_1 representing an aromatic group preferably chosen from:



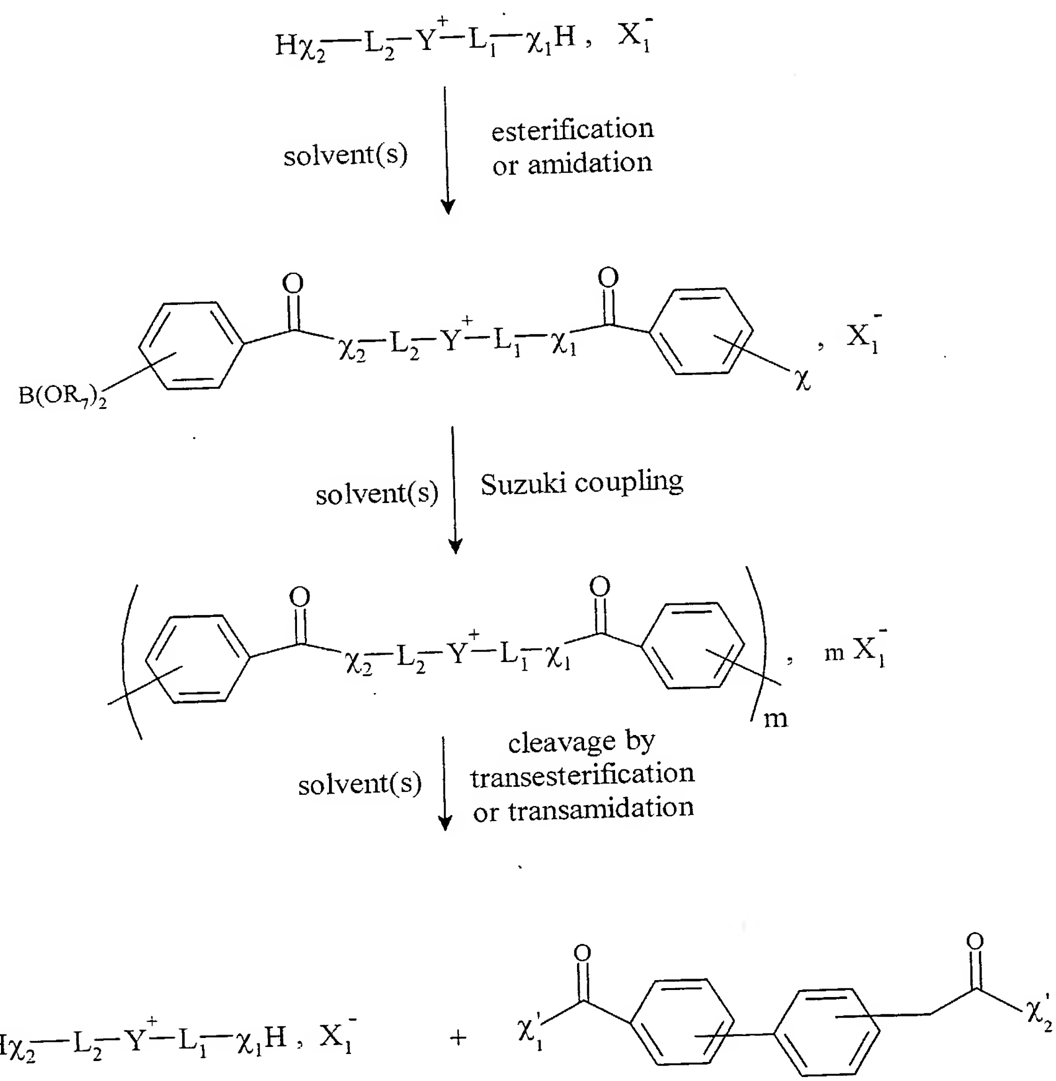
the molecule G being in the form R_2-R_3, R_2 and R_3 being as defined above, and corresponding in particular to the following formula:



in which χ_2 represents either an $-OR_g$ group, R_g representing a hydrogen atom or an alkyl group comprising from 1 to 20 carbon atoms, or an $-NR_hR_u$ group, R_h and R_u representing independently of one another a hydrogen atom, an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms,

Ar_1 is as defined above.

The present invention also relates to the use as defined above, for the implementation of Suzuki coupling, according to the following reaction diagram:



m representing an integer comprised between 1 and 50,

Y^+ representing an onium cation as defined above, of formula $(R_b)_{x-2}A^+$ in which x represents an integer equal to 3 or 4 according to the nature of A^+, namely an

ammonium, phosphonium or sulphonium cation respectively, R_b represents an alkyl group comprising from 1 to 20 carbon atoms, an aryl group comprising from 6 to 30 carbon atoms or an aralkyl or alkaryl group comprising from 6 to 30 carbon atoms, said abovementioned alkyl, aryl, aralkyl or alkaryl groups being non-functional, and in which Λ^+ represents an ammonium, imidazolium, phosphonium or sulphonium cation, Y^+ representing in particular an alkylammonium, alkylphosphonium or alkylsulphonium cation, and preferably being a tetraalkylammonium, tetraalkylphosphonium, dialkylimidazolium, trialkylsulphonium cation,

L_1 and L_2 representing an arm, identical or different, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl group comprising from 6 to 30 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 1 to 10,

X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

χ_1 and χ_2, identical or different, representing an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

χ representing a leaving group preferably chosen from Cl, Br, I, OTf, $O\text{-}CO_2R^5$ or $OSO_3\text{-}R^5$, R^5 representing an alkyl group comprising from 1 to 10 carbon atoms or an aralkyl group comprising from 6 to 30 carbon atoms,

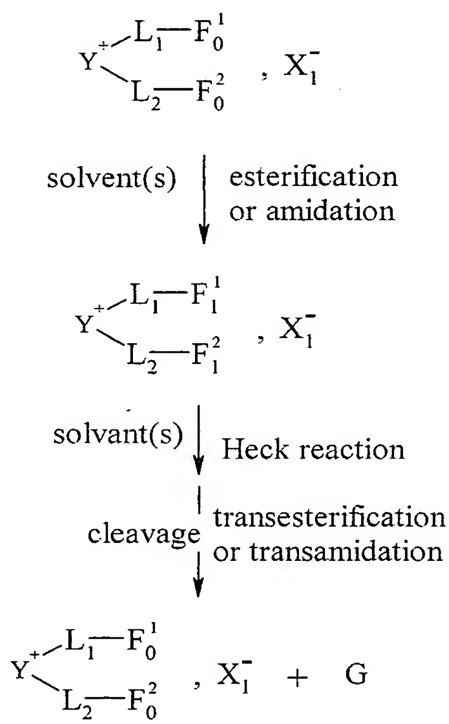
R_7 representing a hydrogen atom, a branched or non-branched alkyl, or cycloalkyl group, comprising from 1 to 12 carbon atoms, or an aryl group, comprising from 6 to 30 carbon atoms,

χ'_1 and χ'_2, identical or different, representing either an $-OR_g$ group, R_g representing a hydrogen atom or an alkyl group comprising from 1 to 20 carbon atoms, or an $-NR_hR_u$ group, R_h and R_u representing independently of one another a hydrogen

atom, an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms.

The use of a plurifunctional salt within the framework of the Suzuki reaction makes it possible to increase the productivity of the solutions used. Moreover, the arms can be functionalized differently and allow either intramolecular reactions, or cascade reactions, or multicomponent reactions.

The present invention relates to the use as defined above, for the implementation of the Heck reaction, according to the following reaction diagram:



Y^+ representing an onium cation as defined above, of formula $(R_b)_{x-2}A^+$ in which x represents an integer equal to 3 or 4, R_b represents an alkyl group comprising from 1 to 20 carbon atoms, an aryl group comprising from 6 to 30 carbon atoms or an aralkyl or alkaryl group comprising from 6 to 30 carbon atoms, said abovementioned alkyl, aryl, aralkyl or alkaryl groups being non-functional, and in which A^+ represents an ammonium, imidazolium, phosphonium or sulphonium cation, Y^+ representing in particular an alkylammonium, alkylphosphonium or alkylsulphonium cation, and preferably being a tetraalkylammonium, tetraalkylphosphonium, dialkylimidazolium, trialkylsulphonium cation, A^+ representing an ammonium or phosphonium cation when x = 4 and a sulphonium cation when x = 3,

L_1 and L_2, identical or different, representing an arm, in particular a linear or branched alkyl group comprising from 1 to 20 carbon atoms, or an optionally functional aralkyl or alkaryl group, comprising from 1 to 20 carbon atoms, and preferably being a linear alkyl group, preferably a linear alkyl group of type $(CH_2)_r$, r varying from 1 to 20, and preferably from 2 to 10,

X_1^- being as defined above, and being in particular Cl^-, Br^-, I^-, $CF_3CO_2^-$, $CH_3CO_2^-$, BF_4^-, PF_6^-, $CF_3SO_3^-$, $^-N(SO_2CF_3)_2$, SO_4^{2-}, $R_1SO_4^-$, SbF_6^-, $R_1SO_3^-$, FSO_3^-, PO_4^{3-}, R_1 representing an alkyl group comprising from 1 to 20 carbon atoms,

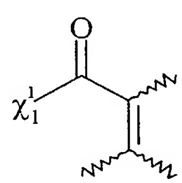
the solvent or solvents being chosen from: dichloromethane, tetrahydrofuran, dioxane, acetonitrile, dimethylformamide, dimethylacetamide, N-methylpyrrolidinone, propionitrile, acetone, toluene, chlorobenzene, nitrobenzene, dichlorobenzene, nitromethane, nitroethane, or a mixture of these solvents,

the functions F_0^1, F_1^1, F_0^2 and F_1^2 being as defined below:

– F_0^1 corresponds to a $-\chi^1_1H$ group, in which χ^1_1 represents an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

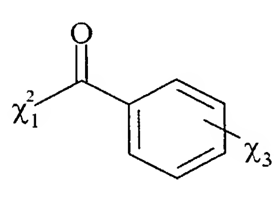
– F_0^2 corresponds to a $-\chi^2_1H$ group, in which χ^2_1 represents an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms,

– F_1^1 corresponds to the following formula:



χ^1_1 being as defined above,

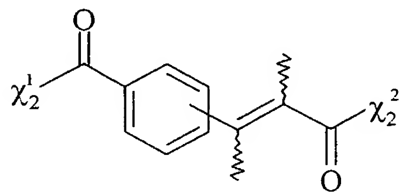
– F_1^2 corresponds to the following formula:



χ^2_1 representing an oxygen atom or an $-NR_f$ group, R_f corresponding to a linear or branched alkyl group, comprising from 1 to 20 carbon atoms, or an aryl group comprising from 6 to 30 carbon atoms, and

χ_3 representing a leaving group, in particular chosen from the I, Cl and Br halides, the mesylate, tosylate, triflate, sulphonate, sulphate or phosphate groups,

G corresponding to the following formula:



in which χ_2^1 and χ_2^2, identical or different, represent either an $-OR_g$ group, R_g representing a hydrogen atom or an alkyl group comprising from 1 to 20 carbon atoms, or an $-NR_hR_u$ group, R_h and R_u representing independently of one another a hydrogen atom, an alkyl group comprising from 1 to 20 carbon atoms or an aryl group comprising from 6 to 30 carbon atoms.

The use of a plurifunctional salt within the framework of the Heck reaction makes it possible to increase the productivity of the solutions used. Moreover, the arm can be functionalized differently and allow either intramolecular reactions, or cascade reactions, or multicomponent reactions.

DESCRIPTION OF THE FIGURES

Figure 1 represents proton NMR spectra recorded at 200 MHz in acetone D6, corresponding to the monitoring of the Heck coupling reaction between salt **5** (Y = $(Me)_3N$, n = 0) and iodobenzene. The spectrum at the bottom corresponds to the starting product **5d** in acetone D6 and the spectrum at the top to the incoming crude product **24d** in the acetone D6.

Figure 2 represents a chromatogram corresponding to the mixture of the three methyl esters **27a** to **27c** the mass spectra of which are described in Table 7.

Figure 3 represents a chromatogram corresponding to the mixture of the seven biaryl methyl esters **29a** to **29g** the mass spectra of which are described in Table 8.

Figure 4 represents a chromatogram corresponding to the mixture of the nine biaryl methyl esters **31a** to **31i** the mass spectra of which are described in Table 10.

Figure 5 represents a chromatogram corresponding to the mixture of the nine biaryl ethyl esters **32a** to **32i** the mass spectra of which are described in Table 11.

Figure 6 represents a chromatogram corresponding to the mixture of the nine biaryl propyl esters **33a** to **33i** the mass spectra of which are described in Table 12.

Figure 7 represents of the proton NMR spectra recorded at 200 MHz in acetone D6, corresponding to the monitoring of the Sonogashira reaction starting with salt **6b**. The spectrum at the bottom corresponds to the coupling product of **6b** with heptynol in acetone D6 and the spectrum at the top to the starting product **6b** in acetone D6.

Figure 8 represents a chromatogram corresponding to the mixture of the five acetylenic methyl esters **35a** to **35e** the mass spectra of which are described in Table 17.

Figure 9 represents a chromatogram corresponding to the mixture of the five acetylenic ethyl esters **36a** to **36e** the mass spectra of which are described in Table 18.

Figure 10 represents a chromatogram corresponding to the mixture of the five acetylenic propyl esters **37a** to **37e** the mass spectra of which are described in Table 19.

Figure 11 represents a chromatogram corresponding to the mixture of the five acetylenic butyl esters **38a** to **38e** the mass spectra of which are described in Table 20.

Figure 12 represents a chromatogram corresponding to the mixture of the six alcohols **40a** to **40f** the mass spectra of which are described in Table 22.

Figure 13 represents proton NMR spectra recorded at 200 MHz in acetone D6, corresponding to the monitoring of the Grieco reaction carried out on an onium salt. The spectrum at the top corresponds to the starting product **7g** and the spectrum at the bottom corresponds to the incoming product **42**.

Figure 14 represents the HPLC chromatogram of the products **47a** to **47e** (Sonogashira coupling products).

Figure 15 represents the GC/MS chromatogram of the mixture of tetrasubstituted olefins **49a** to **49e** (Table 26).

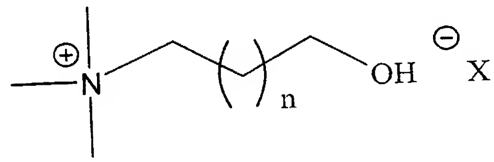
Figure 16 represents a chromatogram of the Suzuki coupling product **14a** (X = Cl) with phenylboronic acid after transesterification by methanol.

Figure 17 represents proton NMR spectra recorded at 200 MHz in acetone D6, corresponding to the monitoring of the cycloaddition reaction between acryloyl bis-ester **13** and cyclopentadiene. The spectrum at the top corresponds to the starting product **13** and the spectrum at the bottom corresponds to the cycloaddition product obtained after reaction with cyclopentadiene.

EXPERIMENTAL PART – PREPARATION OF THE COMPOUNDS

I) SYNTHESIS OF THE FUNCTIONALIZED SALTS:

1/ Ammonium salts 1:

1	
1a	**n = 0; X = NTf_2**
1b	**n = 1; X = Cl**
1c	**n = 1; X = PF_6**
1d	**n = 1;X = BF_4**
1e	**n = 1; X = NTf_2**
1f	**n = 2; X = Cl**
1g	**n = 2; X = NTf_2**
1h	**n = 2; X = OTf**
1i	**n = 3; X = Cl**
1j	**n = 3; X = NTf_2**

* **1a:**

A solution of 2 g (0.01 mmol) of trimethyl-2-hydroxyethylammonium in 1 ml of water is added to a solution of 1 g (0.018 mmol) of lithium bis-trifluoromethanesulphonamidide. The mixture is stirred for 2 hours. The two phases obtained are separated, and the aqueous phase is extracted twice with 15 ml of methylene chloride. The solvent is then evaporated off and the product is dried under vacuum.

Colourless viscous oil **Yield** = 90 %

^{1}H NMR (200 MHz, Acetone D_6): 3.35 (s, 9H); 4.14-4.40 (m, 2H); 4.05-4.63(m, 2H).

^{13}C NMR (50 MHz, Acetone D_6): 55.02 (t; $J_{C\text{-}N}$=4.03 Hz); 57.23; 68.91; 121.05 (q, J=321.2 Hz).

* **1b:**

25 g (0.1 mol) of 3-chloropropanol, 30 ml of a 45% solution of trimethylamine in water (0.2 mol) and 100 ml of acetonitrile are taken to reflux for 36 hours. The solvent

is then evaporated off under vacuum and the white solid obtained is washed twice with 30 ml of ether.

White solid **Yield** = 82% **Mp** = 158-160°C

^{1}H NMR (200 MHz, D_2O): 1.80-2.05 (m, 2H); 3.00 (s, 9H); 3.20-3.41 (m, 2H); 3.60 (t, 2H, J = 7.1 Hz)

^{13}C NMR (50 MHz, D2O): 25.68; 53.31 (t, J_{C-N}= 4.1 Hz); 58.52; 64.52.

Mass Spectrometry (FAB) for $C_{12}H_{32}N_2O_2Cl$

Theoretical mass calculated for $(2C^+, Cl^-)^+$ 271.2152

Mass found 271.2149

* **1c**:

A mixture of a solution of 10 g (65.3 mol) of N,N',N''-trimethyl-3-hydroxypropylammonium chloride (**1b**) in 15 ml of water and 13.23 ml (0.15 mol) of hexafluorophosphoric acid in solution at 60% in water is stirred at ambient temperature for 2 hours. The medium immediately becomes heterogeneous and the precipitate formed is filtered and washed with ether. The white solid obtained is dried under vacuum.

White solid **Yield** = 67% **Mp** = 124-126°C

^{1}H NMR (200 MHz, CD_3CN): 1.70 (m, 2H); 2.82 (s, 9H); 3.15 (m, 2H); 3.40 (t, 2H, J = 6.1 Hz).

^{13}C NMR (50 MHz, CD_3CN): 25.44; 52.59 (t; J = 4.2 Hz); 57.67; 64.26 (t, J = 3.8 Hz). -

Mass spectrometry (FAB) for $C_{12}H_{32}N_2O_2F_6P$

Theoretical mass calculated for $(2C^+, PF_6^-)^+$ 381.2106

Mass found 381.2098

* **1d**:

A mixture of a solution of 10 g (65 mmol) of N,N',N''-trimethyl-3-hydroxypropylammoinum chloride (**1b**) in 15 ml of water and 9.1 ml (0.15 mol) of 50% tetrafluoroboric acid in water is stirred at ambient temperature. The medium remains homogeneous. After 12 hours, the water is evaporated to dryness and the white solid obtained is washed twice with 15 ml of anhydrous ether.

White solid **Yield** = 82% **Mp** = 110-112°C

^1H NMR (200 MHz, Acetone D_6): 2.10-2.241 (m, 2H); 3.05 (s, 9H); 3.24-3.45 (m, 2H); 3.61 (t, J = 7.1 Hz, 2H).

^{13}C NMR (50 MHz, Acetone D_6): 27.52; 53.35 (t; J_{C-N} = 4.1 Hz); 58.25; 64.58.

* **<u>1e</u>:**

10 g of ammonium salt (**<u>1b</u>**) (65.3 mmol) is dissolved in 10 ml water. This solution is added to 20 g of lithium bis-trifluoromethanesulphonamide (71.9 mmol) in 10 ml of water. The mixture is stirred for 2 hours at ambient temperature. The two phases obtained are separated, and the aqueous phase is extracted twice with 15 ml of methylene chloride. Finally the solvent is evaporated off and the product is dried under vacuum.

Colourless viscous oil **Yield** = 86%

^1H NMR (200 MHz, Acetone D_6): 2.00-2.21 (m, 2H); 3.25 (s, 9H); 3.50-3.80 (m, 4H).

^{13}C NMR (50 MHz, Acetone D_6): 29.14; 54.27 (t; J_{C-N} = 4.1 Hz); 60.05; 66.09; 121.05 (q, J = 321.2 Hz).

* **<u>1f</u>:**

2 ml (23.90 mmol) of 3-chloropropanol and 4 ml of a 45% solution of trimethylamine in water (40 mmol) are placed in a 250 ml flask. The mixture is then taken to reflux for 24 hours. The solvents are then evaporated under vacuum. The white solid obtained is washed twice with 30 ml of ether.

White solid **Yield** = 94% **Mp** = 118-120°C

^1H NMR (200 MHz, D_2O): 1.6-1.78 (m, 2H); 1.85-2.05 (m, 2H); 3.25 (s, 9H); 3.4-3.5 (m, 2H); 3.60 (t, 2H, J = 7.2 Hz)

^{13}C NMR (50 MHz, D2O): 19.50; 28.43; 53.18 (t, J_{C-N} = 4.1 Hz); 61.11; 66.66.

* **<u>1g</u>:**

A solution of 1 g (0.01mole) of ammonium salt (**<u>1f</u>**) in 1 ml of water is prepared in a beaker. In another beaker, 2 g (0.018 mmol) of lithium bis-trifluoromethanesulphonamide is dissolved in the same way. The two solutions are mixed together and stirred for 2 hours at ambient temperature to ensure total exchange. The two phases obtained are separated in a separatory funnel, and the aqueous phase is

extracted twice with 15 ml of methylene chloride. Finally the solvent is evaporated off and the product is dried under vacuum.

Colourless viscous oil **Yield** = 86%

^{1}H NMR (200 MHz, Acetone D_6): 1.5-1.65 (m, 2H); 1.9-2.2 (m, 2H); 3.3 (s, 9H); 3.50-3.65 (m, 5H).

^{13}C NMR (50 MHz, Acetone D_6): 20.91; 30.47; 53.99 (t; $J_{C\text{-}N}$ = 4.03 Hz); 61.88; 67.90; 121.05 (q, J = 321.2 Hz)

* **1h:**

4.71 g (37.4 mmol) of methyltriflate at 0°C is added to a solution of 4 g (34 mmol) of N,N'-dimethylamino-1-butanol in 10 ml of acetonitrile. It is allowed to reach ambient temperature under stirring and is then stirred for 2 hours. After this, the solvent is evaporated to dryness and the colourless oil obtained is washed with 3 x 10 ml of ether and dried under vacuum.

Colourless oil **Yield** = 97%

^{1}H NMR (200 MHz, Acetone D_6): 1.65-1.80 (m, 2H); 1.90-2.00 (m, 2H); 3.12 (s, 9H); 3.3-3.5 (m, 2H); 3.68 (t, 2H, J = 6.13 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 28.36; 28.99; 51.93 (t; $J_{C\text{-}N}$ = 4.03 Hz); 60.47; 68.75 (t; $J_{C\text{-}N}$ = 4.03 Hz); 121.05 (q, J = 321.2 Hz)

* **1i:**

5 g (36 mmol) of 6-chlorohexanol, 10 ml of a 45% solution of trimethylamine in water (0.1 mol) and 100 ml of acetonitrile to homogenize the medium are placed in a 250 ml flask. The mixture is then taken to reflux for 36 hours. The water/acetonitrile mixture is evaporated under vacuum and the white solid obtained is washed twice with 30 ml of ether.

White solid **Yield** = 62% **Mp** = 178-180°C

^{1}H NMR (200 MHz, MeOH): 1.30-1.65 (m, 6H); 1.80-1.95 (m, 2H); 3.18 (s, 9H); 3.4-3.6 (m, 2H); 3.55 (t, 2H, J = 6.1 Hz).

^{13}C NMR (50 MHz, MeOH): 22.93; 25.48; 26.15; 32.35; 52.60 (t; J = 4.1 Hz); 61.67; 66.76.

* **<u>1j</u>:**

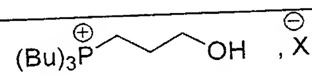
A mixture of a solution of 10 g (51.2 mmol) of N,N',N''-trimethyl-6-hydroxybutylammonium chloride (**<u>1i</u>**) in 15 ml of water and 18.7g (6.66 mmol) of lithium bis-trifluoromethanesulphonamide is stirred at ambient temperature. The medium immediately becomes heterogeneous, and the two phases are separated in a separatory funnel. The colourless oil obtained is then washed twice with 3 ml of water and dried at 50°C under high vacuum.

Colourless oil **Yield** = 93%

^{1}H NMR (200 MHz, Acetone, D6): 1.41-1.60 (m, 6H); 1.88-2.01 (m, 2H); 3.30 (s, 9H); 3.50-3.65 (m, 4H); 3.55(t, 2H, J = 6.1 Hz).

^{13}C NMR (50 MHz, Acetone, D6): 23.02; 25.60; 26.22; 53.01 (t; J = 4.1 Hz); 61.73; 66.99; 121.05 (q, J = 324.2 Hz).

2/ Phosphonium salts <u>2</u>:

<u>2</u>	

<u>2a</u>	**X = Cl**
<u>2b</u>	**X = NTf_2**

* **<u>2a</u>:**

2 ml (23.90 mmol) of 3-chloropropanol and 7.2 ml (28.68 mmol) of tributylphosphine are taken to reflux for 14 h. The excess of tributylphosphine is then eliminated by washing in ether (3 × 10 ml).

Colourless oil **Yield** = 72%

^{1}H NMR (200 MHz, D_2O): 0.90 (t; 9H; J = 5.57 Hz); 1.30-1.60 (m, 12H); 1.65-1.85 (m, 2H); 2.05-2.30 (m, 8H); 3.55-3.70(m, 2H).

^{13}C NMR (50 MHz, D_2O): 13.15; 14.91; 15.90; 17.57; 18.53; 23.10, 23.59; 23.89; 34.62; 42.52; 58.77; 61.32; 61.64.

* **<u>2b</u>:**

2 g (6.97 mmol) of lithium bis-trifluoromethanesulphonamide and 1 g (3.36 mmol) of tributyl-3-hydroxypropyl phosphonium chloride (**<u>2a</u>**) are dissolved in 3 ml of water. The two solutions are then mixed and stirred for 2 h at ambient temperature.

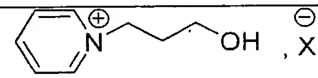
The aqueous phase is extracted twice with 15 ml of methylene chloride and the organic phases are re-assembled and dried over $MgSO_4$. The solvent is then evaporated to dryness and the product obtained is dried under vacuum.

Colourless oil **Yield** = 90%

^{1}H NMR (200 MHz, Acetone D_6): 0.75 (t; 9H; J = 7.13); 1.22-1.60 (m, 12H); 1.61-1.82 (m, 2H); 2.12-2.34 (m, 8H); 3.45-3.60 (m, 2H); 3.8 (t, 1H, J = 5 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 13.99; 16.06; 17.05; 18.90; 19.86; 24.29; 24.38; 24.81; 25.12; 25.61; 25.70; 62.05; 62.35; 121.05 (q, J_{CF} = 374.2 Hz)

3/ Pyridinium salts 3:

3	

3a	**X = Cl**
3b	**X = NTf_2**

* **3a:**

2 ml (23.9 mmol) of 3-chloropropanol and 6 ml of pyridine are introduced into a 100 ml flask. The reaction mixture is heated to 80°C overnight. The excess pyridine is eliminated by washing with 3 x 10 ml of ether. Finally, the product is crystallized from acetone.

White solid **Yield** = 73 % **Mp** = 68-70°C

^{1}H NMR (200 MHz, D_2O): 2.1-2.3 (m, 2H); 3.6 (t, J = 5.99 Hz, 2H); 3.75 (t, J = 7.19 Hz, 2H); 8.01 (t, J = 7.04 Hz, 2H); 8.55 (t, J = 9.97 Hz, 1H); 8.83 (d, J = 6.04Hz, 2H)

^{13}C NMR (50 MHz, D_2O): 33.14; 58.22; 59.51; 128.72; 144.89; 146.12

* **3b:**

2 g (6.97 mmol) of lithium bis-trifluoromethane-sulphonamide are dissolved in 3 ml of water in a beaker. In the same way, approximately 1 g (5.76 mmol) of 3-hydroxypropylpyridinium chloride (3a) is dissolved in water in another beaker, then the two solutions are mixed and stirred for two hours.

The content of the beaker is poured into a separatory funnel. The aqueous phase is extracted twice with 15 ml of methylene chloride. The organic phases are collected

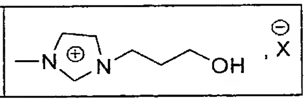
and dried over $MgSO_4$. The solvent is then evaporated to dryness and the product is dried under vacuum.

Colourless oil **Yield** = 90%

^{1}H NMR (200 MHz, Acetone): 2.03-2.21 (m, 2H); 3.5 (t, J = 6.1Hz, 2H); 3.8 (t, J = 6.9 Hz, 1H); 4.73 (t, J = 7Hz, 2H); 8.1 (t, J = 7 Hz, 2H); 8.52 (t, J = 9.8 Hz, 1H); 8.98(d, J = 6.1 Hz, 2H).

^{13}C NMR (50 MHz, Acetone): 34.57; 58.95; 60.95; 121.37 (q, J_{C-F} = 320.9 Hz); 129.67; 146.46; 147.11

4/ Imidazolium salts <u>4</u>:

<u>4</u>	

<u>4a</u>	**X = Cl**
<u>4b</u>	**X = NTf_2**

* **<u>4a</u>:**

2 ml (23.90 mmol) of 3-chloropropanol and 2.87 g (35 mmol) of N-methylimidazole are introduced into a 100 ml flask. The reaction mixture is heated to 80°C overnight. The excess of the N-methylimidazole is eliminated by washing with ether (3 × 10 ml) and the white solid obtained is dried under vacuum.

White solid **Yield** = 80 %

^{1}H NMR (200 MHz, D_2O): 1.96-2.25 (m, 2H); 3.55 (t, 2H, J = 6.11 Hz); 3.85 (s, 3H); 4.15 (t, 2H, J = 7.12 Hz); 7.43 (apparent t, 1H, J = 1.73 Hz); 7.48 (apparent t, 1H, J = 1.74 Hz); 8.75 (s, 1H)

^{13}C NMR (50 MHz, D_2O): 32.87; 35.40; 47.23; 58.29; 123.03; 124.26; 137.06

* **<u>4b</u>:**

2 g (6.97 mmol) of $LiNTf_2$ is dissolved in 3 ml of water in a beaker. In the same way, approximately 1 g of imidazolium chloride **<u>4a</u>** is dissolved in water in another beaker. The two solutions are mixed, and stirred for two hours.

The content of the beaker is poured into to a separatory funnel. The aqueous phase is extracted twice with 15 ml of methylene chloride. The organic phases are collected and dried over $MgSO_4$. The solvent is then evaporated to dryness and the product is dried under vacuum.

colourless oil **Yield** = 90%

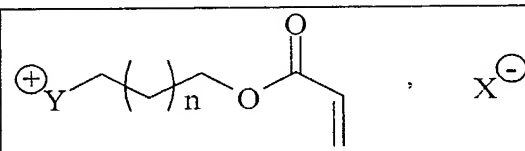
***^{1}H NMR (200 MHz, Acetone)*:** 2.15-2.21 (m, 2H); 3.65 (t, 2H, J = 6.11 Hz); 4.05 (s, 3H); 4.15 (t, 2H, J = 7.12 Hz); 7.68 (apparent t, 1H, J = 1.73 Hz); 7.73 (apparent t, 1H, J = 1.74 Hz); 8.95 (s, 1H)

^{13}C NMR (50 MHz, Acetone): 32.32; 35.92; 47.01; 58.35; 121.37 (q, $J_{C\text{-}F}$ = 320.9 Hz); 123.25; 124.01; 136.50

II) FUNCTIONALIZATION OF THE PREVIOUS SALTS:

1/ Acrylic ester 5:

General procedure for esterification with acrylic acid:

5	

5	Y	n	X
5a	$N(Me)_3$	0	NTf_2
5b	$N(Me)_3$	1	Cl
5c	$N(Me)_3$	1	BF_4
5d	$N(Me)_3$	1	NTf_2
5e	$N(Me)_3$	2	NTf_2
5f	$P(Bu)_3$	1	NTf_2
5g	Py	1	NTf_2
5h	Im	1	NTf_2

A solution of the onium salt and 3 equivalents of acryloyl chloride in acetonitrile is heated to 80°C for 2 hours in the presence of 5 equivalents of solid K_2CO_3. The reaction mixture is then placed under vacuum at 40°C in order to eliminate the solvent and the excess of the reagent. The onium acrylate is then extracted with methylene chloride.

* **5a**:

pink oil **Yield** = 90%

^{1}H NMR (200 MHz, Acetone D_6): 3.5 (s, 9H); 4.03-4.40 (m, 2H); 4.73-4.85 (m, 2H); 6.05 (dd, 1H, J_1 = 1.92 Hz, J_2 = 10.5 Hz); 6.25 (dd, 1H, J_1 = 10.5 Hz, J_2 = 17.3 Hz); 6.45 (dd, 1H, J_1 = 1.9 Hz, J_2 = 17.3 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 54.01 (t, J = 4.2 Hz); 58.25; 65.23; 121.05 (q, J_{CF} = 374.2 Hz); 128.80; 132.24; 165.46

* **5b**:

White solid **Yield** = 100% **Mp** = 175-177°C

^{1}H NMR (200 MHz, Acetone D_6): 2.15-2.20 (m, 2H); 3.15 (s, 9H); 3.48-3.52 (m, 2H); 4.18 (t, 2H, J = 6.0 Hz); 5.75 (dd, 1H, J_1 = 1.92 Hz, J_2 = 10.5 Hz); 6.15 (dd, 1H, J_1 = 10.5 Hz, J_2 = 17.3 Hz); 6.15 (dd, 1H, J_1 = 1.9 Hz, J_2 = 17.3 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 21.74; 52.23 (t, J = 4.2 Hz); 60.44 (t, J = 3.02); 62.6; 127.41; 130.65; 165.04

* **5c**:

Colourless oil **Yield** = 93%

1H NMR (200 MHz, Acetone D_6): 2.28-3.31 (m, 2H); 3.32 (s, 9H); 3.06-3.15 (m, 2H); 4.52 (t, 2H, J = 6.6 Hz); 5.80 (dd, 1H, J_1 = 1.9 Hz, J_2 = 10.0 Hz); 6.05 (dd, 1H, J_1 = 18.3 Hz, J_2 = 10.0 Hz); 6.15 (dd, 1H, J_1 = 1.9 Hz, J_2 = 18.3 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 22.81; 53.28; 61.46; 63.83; 128.51; 131.72; 167.31

* **5d**:

Colourless oil **Yield** = 100%.

^{1}H NMR (200 MHz, Acetone D_6): 2.22-2.25 (m, 2H); 3.25 (s, 9H); 3.60-3.75 (m, 2H); 4.15 (t, 2H, J = 6.0 Hz); 5.80 (dd, 1H, J_1 = 1.92 Hz; J_2 = 10.68 Hz); 6.05 (dd, 1H, J_1 = 17.2; J_2 = 10.7); 6.15 (dd, 1H, J_1 = 1.9 Hz; J_2 = 17.2 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 29.17; 54.16 (t, J = 4.0); 65.16; 65.23; 121.05 (q, J_{CF} = 374.2 Hz); 129.40; 132.15; 165.61

^{19}F NMR (282 MHz, Acetone D_6): – 79.8

Mass spectrometry (FAB) for $C_9H_{18}NO_2$

Theoretical mass calculated for (C^+)	172.1338
Mass found	172.1346

* **5e:**

Colourless oil **Yield** = 77%

^{1}H NMR (200 MHz, Acetone D_6): 1.7-1.9 (m, 2H); 2.00-2.20 (m, 2H); 3.40 (s, 9H); 3.58-3.72 (m, 2H); 4.25 (t, 2H, J = 6.0 Hz); 5.80 (dd, 1H, J_1 = 1.92 Hz; J_2 = 10.68 Hz); 6.05 (dd, 1H, J_1 = 17.2; J_2 = 10.7); 6.15 (dd, 1H, J_1 = 1.9 Hz; J_2 = 17.2 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 20.86; 26.44; 53.99; 64.52; 67.37; 122.19 (q, J_{CF} = 374.2 Hz); 129.69; 131.83; 166.99

* **5f:**

Colourless oil **Yield** = 77%

^{1}H NMR (200 MHz, Acetone D_6): 1 (t, 9H, J = 7.2 Hz); 1.45-1.85 (m, 12H); 2.10-2.28 (m, 2H); 2 .48-2.7 (m, 8H); 4.3 (t, 2H, J = 6.27 Hz); 5.58 (dd, 1H, J_1 = 0.3 Hz; J_2 = 1.96 Hz); 6.18 (dd, 1H, J_1 = 17.16 Hz; J_2 = 0.3 Hz); 6.4 (dd, 1H, J_1 = 17.16 Hz; J_2 = 1.97 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 13.09; 15.10; 16.09; 17.84; 18.80; 21.15; 21.22; 23.38; 23.47; 23.86; 24.18; 63.77; 64.11; 121.05 (q, J_{CF} = 374.2 Hz); 128.63; 131.12; 165.74

* **5g:**

Colourless oil **Yield** = 80%

^{1}H NMR (200 MHz, Acetone D_6): 2.15-2.27 (m, 2H); 3.8 (t, J = 6.1 Hz, 2H); 4.96 (t, J= 6.8 Hz, 2H); 5.54 (dd, 1H, J_1 = 0.5 Hz; J_2 = 2 Hz); 6.18 (dd, 1H, J_1 = 17.2 Hz; J_2 = 0.3 Hz); 6.4 (dd, 1H, J_1 = 17.2 Hz; J_2 = 2 Hz); 8.1 (t, J = 7 Hz, 2H); 8.52 (t, J = 9.8 Hz, 1H); 8.98 (d, J = 6.2 Hz, 2H)

^{13}C NMR (50 MHz, Acetone D_6): 30.39; 59.98; 61.42; 121.05 (q, J_{CF} = 374.2 Hz); 128.75; 128.98; 131.38; 145.48; 146.50; 165.78

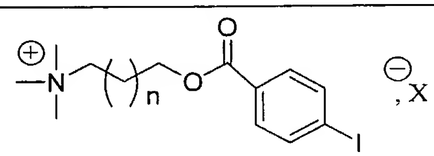
* **5h**:

Colourless oil **Yield** = 85 %

[1]H NMR (200 MHz, Acetone D_6): 2.3-2.5 (m, 2H); 4.15 (s, 3H); 4.28 (t, 2H, J = 6.03 Hz); 4.63 (t, 2H, J = 6.99 Hz); 5.95 (dd, 1H, J_1 = 1.92; J_2 = 10.68); 6.18 (dd, 1H, J_1 = 17.2 Hz; J_2 = 10.7 Hz); 6.4 (dd, 1H, J_1 = 1.9 Hz; J_2 = 17.2 Hz); 7.8 (apparent t, 1H, J = 1.70 Hz); 7.95 (apparent t, 1H, J = 1.82 Hz); 9.2 (s, 1H)

[13]C NMR (50 MHz, Acetone D_6): 29.32; 36.17; 47.38; 61.36; 121.05 (q, J_{CF} = 374.2 Hz); 122.97; 124.30; 128.44; 131.31; 136.948; 166.07

2/ 4-iodobenzoic esters 6:

6	

6	n	X
6a	**2**	**I**
6b	**2**	**NTf_2**
6c	**2**	**PF_6**
6d	**2**	**BF_4**
6e	**2**	**OTf**
6f	**0**	**BF_4**
6g	**1**	**NTf_2**

* **6a**:

1.1 ml (13.15 mmol) of methyl iodide is added dropwise at 0°C to a solution of 4g (10.96 mmol) of 3-dimethyl-aminopropyl para-iodobenzoate in 10 ml of acetonitrile. The white solid thus formed is filtered then washed with 3 x 10 ml of ether.

White solid **Yield** = 99% **Mp** = 248-250°C

[1]H NMR (200 MHz, Acetone D_6): 1.9-2.05 (m, 4H); 3.20 (s, 9H); 3.42-3.55 (m, 2H); 4.45 (t, 2H, J = 6.05 Hz); 7.8 (d, 2H, J = 8.73 Hz); 7.95 (d, 2H, J_1 = 8.76 Hz)

[13]C NMR (50 MHz, Acetone D_6): 19.89; 25.45; 53.37 (t, J_{C-N} = 4.1 Hz); 65.13; 66.42; 101.57; 131.19; 131.45; 138.38; 166.78

Mass spectrometry (FAB) for $C_{28}H_{42}N_2O_4I_3$

Theoretical mass calculated for $(2C^+, I^-)^+$	851.03
Mass found	851.10

* <u>**6b**</u>:

A 2.65 mmol of $LiNTf_2$ in solution in water is added to a solution of 1 g (2.04 mmol) of **<u>6a</u>** in 30 ml of the water/acetone mixture. After stirring at ambient temperature for 2 hours, the solvent is evaporated off and the salt extracted with 3 × 10 ml of methylene chloride. After evaporation of the latter, a white solid is obtained.

White solid **Yield** = 90% **Mp** = 48-50°C

^1H NMR (200 MHz, Acetone D_6): 1.82-2 (m, 2H); 2.1-2.22 (m, 2H); 3.38 (s, 9H); 3.6-3.72 (m, 2H); 4.4 (t, 2H, J = 6.24 Hz); 7.8 (d, 2H, J = 8.73 Hz); 7.95 (d, 2H, J_1 = 8.36 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 26.66; 29.12; 54.12 (t, J_{C-N} = 4.1 Hz); 65.28; 67.40; 101.59; 121.17 (q, J_{C-F} = 320.9 Hz); 131.17; 132.28; 139.23; 166.74

Mass spectrometry (FAB) for $C_{30}H_{42}N_3O_8F_6I_2S_2$

Theoretical mass calculated for $(2C^+, NTf_2^-)^+$	1004.0407
Mass found	1004.0427

* <u>**6c**</u>:

2.65 mmol of (60%) HPf_6 in solution in water is added to a solution of 1 g (2.04 mmol) of ammonium **<u>6a</u>** in 30 ml of the water/acetone mixture. After 2 h of stirring at ambient temperature the solvent is evaporated off and the solid obtained is washed with ether (3 × 10ml).

White solid **Yield** = 96% **Mp** = 204-206°C

^1H NMR (200 MHz, Acetone D_6): 2.05-2.2 (m, 2H); 2.28-2.47 (m, 2H); 3.6 (s, 9H); 3.8-3.97 (m, 2H); 4.6 (t, 2H, J = 6.3 Hz); 8 (d, 2H, J = 8.58 Hz); 8.15 (d, 2H, J_1 = 8.58 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 20.97; 26.65; 54.06 (t; J = 4.03 Hz); 65.31; 67.4 (t; J = 3.17 Hz); 101.57; 131.19; 132.32; 139.23; 166.75

Mass spectrometry (FAB) for $C_{28}H_{42}N_2O_4F_6I_2P$

Theoretical mass calculated for $(2C^+, PF_6^-)^+$	869.0876
Mass found	869.0879

* **6d**:

2.65 mmol of 40 % HBF_4 in solution in water is added to a solution of 1 g (2.04 mmol) of **6a** in 3 ml of water. After the former has been added, the formation of a white solid is noted. The reaction mixture is stirred for two hours at ambient temperature. The white solid obtained after filtration is washed with water (in order to eliminate the excess of HBF_4) then twice with 30 ml of ether and finally dried under vacuum.

White solid **Yield** = 86% **Mp** = 184-186°C

^{1}H NMR (200 MHz, Acetone D_6): 1.90-2.00 (m, 2H); 2.15-2.28 (m, 2H); 3.4 (s, 9H); 3.65-3.80 (m, 2H); 4.42 (t, 2H, J = 6.3 Hz); 7.85 (d, 2H, J = 8.58 Hz); 8.15 (d, 2H, J_1 = 8.58 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 20.96; 26.62; 53.97 (t; J = 4.03 Hz); 65.34; 101.53; 131.22; 132.34; 139.23; 166.73

Mass spectrometry (FAB) for $C_{28}H_{42}N_2O_4F_4I_2B$

Theoretical mass calculated for $(2C^+, BF_4^-)^+$	811.1263
Mass found	811.1259

* **6e**:

1.1 ml (13.15 mmol) of methyl triflate is added dropwise at 0°C to a solution of 1 g (10.96 mmol) of 3-dimethylamino-propyl para-iodobenzoate in 10 ml of acetonitrile. The white solid thus formed is filtered then washed with 3 x 10 ml of ether.

White solid **Yield** = 96% **Mp** = 176-178°C

^{1}H NMR (200 MHz, CD_3CN): 1.8-2.1 (m, 4H); 3.06 (s, 9H); 3.35-3.45 (m, 2H); 4.4 (t, 2H, J = 6.05 Hz); 7.85 (d, 2H, J = 8.58 Hz); 8 (d, 2H, J_1 = 8.58 Hz)

^{13}C NMR (50 MHz, CD_3CN): 19.16; 24.66; 52.50 (t; J = 4.03 Hz); 63.66; 65.62 (t; J = 3.17 Hz); 99.89; 121.17 (q, J_{C-F} = 320.9 Hz); 129.58; 130.59; 137.57; 165.39

Mass spectrometry (FAB) for $C_{29}H_{42}N_2O_7F_3I_2S$

Theoretical mass calculated for $(2C^+, OTf^-)^+$	873.1
Mass found	873.1

* **6f**:

1.5 eq of DCC, 1.5 eq of 4-iodobenzoic acid and 0.2 eq of DMAP is added to a mixture of commercial (2-hydroxy-ethyl)-trimethylammonium chloride in 100 ml of

CH_3CN. The reaction mixture is stirred for 4 hours at ambient temperature then evaporated to dryness. The ester formed is extracted with 3 x 30 ml of water. 1.5 eq of 50% HBF_4 in solution in water is added to this solution. The reaction mixture is stirred for two hours at ambient temperature. The white solid obtained after filtration is washed with water (in order to eliminate the excess of HBF_4) then twice with 30 ml of ether and finally dried under vacuum.

Appearance of the product: White solid Yield = 90% Mp = 200-202°C

^{1}H NMR (CD3CN, 300Mhz): 3.18 (s, 9H); 3.68-3.80 (m, 2H); 4.50-4.73 (m, 2H); 7.78 (dd, J_1=1.9 Hz, J_2=6.7 Hz; 2H); 7.90 (dd, J_1=1.8Hz, J_2=6.6 Hz, 2H).

^{13}C NMR (CD3CN, 75Mhz): 53.40 (t, J=3.8Hz); 58.27; 64.38 (t, J=3.8Hz); 100.57; 128.65; 130.68; 137.76; 164.73.

Mass spectrometry (APCI) for $[C_{12}H_{17}INO_2][BF_4]^-$

Theoretical mass calculated for (C^+)	334.2
Mass found	334.0

* **6g**:

1.5 eq of DCC, 1.1 eq of 4-iodobenzoic acid and 0.2 eq of DMAP are added to a solution of 12.6 mmol of alcohol **1e** in 60 ml of CH_3CN. The reaction mixture is stirred for 4 hours at ambient temperature; filtered and then evaporated to dryness. The white solid obtained is washed several times with ether and finally dried under vacuum.

Appearance of the product: white solid **Yield** = 95 % **Mp** = 48-50°C

^{1}H NMR (300 MHz, Acetone D_6): 2.40-2.60 (m, 2H); 3.47 (S, 9H); 3.80-4.00 (m, 2H); 4.53 (t, 2H, J=5.9 Hz); 7.83 (d, 2H, J=8.3Hz); 7.97 (d, 2H, J=8.3Hz).

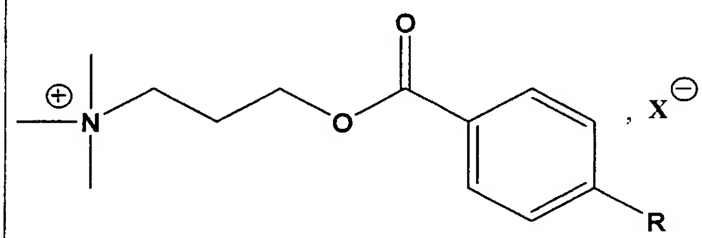
^{13}C NMR (50 MHz, Acetone D_6): 23.07; 53.37 (t, J=3.8Hz); 62.19; 64.46; 100.91; 120.50 (q, J_{CF}=321.2 Hz); 129.97; 131.51; 138.33; 165.75.

Mass spectrometry (APCI) for $[C_{13}H_{19}INO2][C_2NS_2O_4F_6]^-$

Theoretical mass calculated for (C^+)	348.2
Mass found	348.3

3/ 4-substituted benzoic esters 7:

7



N°	X	R
7a	Cl	Br
7b	NTf_2	Br
7c	PF_6	Br
7d	BF_4	Br
7e	BF_4	CH_2=CH-
7f	Cl	NH_2
7g	NTf_2	NH_2
7h	BF_4	O=CH-

* 7a:

2 g (13.1 mmol) of N,N',N''-trimethyl-3-hydroxypropylammonium chloride, 25 ml of acetonitrile, 20 g of K_2CO_3 in powder and 4 g (17.5 mmol) of 4-bromobenzoic acid chloride are introduced into a 250 ml flask. After stirring overnight at ambient temperature, K_2CO_3 is filtered and washed with 3 times 15 ml of methylene chloride and finally evaporated to dryness. It is taken up with water and the excess of 4-bromobenzoic acid, which crystallizes by filtration, is eliminated. The product is then crystallized from acetone after evaporation of water.

White solid **Yield** = 60% **Mp** = 164-166°C

^{1}H NMR (200 MHz, D_2O): 2.21-2.34 (m, 2H); 3.12 (s, 9H); 3.30-3.58 (m, 2H); 4.35 (t, 2H, J = 6.8 Hz); 7.57 (d, 2H, J = 7.4 Hz); 7.80 (d, 2H, J_1 = 7.4 Hz)

^{13}C NMR (50 MHz, D_2O): 22.55; 30.61; 53.34 (t, J_{C-N} = 4.2 Hz); 62.69; 64.41 (t, J_{C-N} = 4.09 Hz); 128.34; 128.66; 131.37; 132.20; 167.84

Mass spectrometry (FAB) for $C_{13}H_{19}NO_2Br$

Theoretical mass calculated for (C^+) 300.0599

Mass found 302.0607

* **7b**:

In this case, synthesis of the substrate has been envisaged according to two approaches: by direct esterification of the N,N,N-trimethyl-3-hydroxypropylammonium bis-trifluoromethanesulphonamide or by metathesis from the corresponding chloride.

Esterification:

4 g (10.5 mmol) of alcohol, 20 ml of acetonitrile, 2 ml of a saturated solution of Na_2CO_3 in water and 4 g (17.5 mmol) of 4-bromobenzoic acid chloride are introduced into a 250 ml flask. The reaction mixture is heated to 60°C overnight. It is then evaporated to dryness, and the residue obtained is dissolved in methylene chloride. This solution is successively washed twice with 20 ml of water, twice with 20 ml of a soda solution (1 N) and finally twice with 20 ml of water. The solution is dried over magnesium sulphate and the solvent is evaporated to dryness. It is taken up in acetone and the traces of acids are eliminated by precipitation at 4°C. After drying under vacuum, a pure white solid is obtained.

Yield = 90 %.

Metathesis

1 g (2.98 mmol) of **1b** is dissolved in 5 ml water in a 100 ml flask. 1.1 g (3.19 mmol) of lithium bis-trifluoromethanesulphonamide ($LiNTf_2$) in solution in 3 ml of water is added to this solution. The reaction mixture is stirred for 2 hours at ambient temperature before extracting the product with 20 ml of methylene chloride. After evaporation of the latter, a white solid is obtained, which is dried under vacuum.

White solid **Yield** = 90% **Mp** = 86-88°C

***^{1}H NMR (200 MHz, Acetone D_6)**:* 2.64-2.83 (m, 2H); 3.59 (s, 9H); 3.96-4.06 (m, 2H); 4.71 (t, 2H, J = 6.76 Hz); 7.90 (d, 2H, J = 8.9 Hz); 8.19 (d, 2H, J = 8.9 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 23.96; 54.24 (t, J_{C-N} = 4.2 Hz); 63.09; 65.35 (t, J_{C-N} = 4.0 Hz); 121.46 (q, J_{C-F} = 322.0 Hz); 128.95; 130.42; 132.58; 133.12; 166.34

Mass spectrometry (FAB) for $C_{28}H_{38}F_6N_3O_8S_2Br_2$

Theoretical mass calculated for ($2C^+$, NTf_2^-) 880.0371

Mass found 880.0375

* **7c**:

0.5 ml (5.7 mmol) of HPF_6 at 60% in water is added to a solution of 1 g (2.98 mmol) of **1b** in 3 ml of water. The reaction mixture is stirred for two hours at ambient temperature. The white solid obtained after filtration is washed with water, then twice with 30 ml of ether, and finally dried under vacuum.

White solid **Yield** = 96% **Mp** = 154-156°C

^{1}H NMR (200 MHz, Acetone D_6): 2.45-2.59 (m, 2H); 3.40 (s, 9H); 3.79-3.85 (m, 2H); 4.50 (t, 2H, j=6.0 Hz); 7.55 (dd, 2H, J_1=1.9 Hz; J_2= 7.7 Hz); 8.00 (dd, 2H, J_1=1.9 Hz; J_2= 7.7 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 22.96; 53.23 (t, J = 4.0 Hz); 62.31; 64.34; 128.06; 129.48; 131.79; 132.25; 165.63

^{19}F NMR (282 MHz, Acetone D_6): -71.6 (d; J = 707.3Hz; P-F)

^{31}P NMR (Acetone, 129.5 MHz) δ: -142 (m, J = 0.7 Hz, P-F_6)

Mass spectrometry (FAB) for $C_{26}H_{38}F_6N_2Br_2O_4P$

Theoretical mass calculated for ($2C^+$, PF_6^-)	745.0840
Mass found	745.0824

* **7d**:

1 ml of 40% HBF_4 in solution in water is added to a solution of 1 g (2.98 mmol) of **1b** in 3 ml of water. After the former has been added, formation of a white solid is noted. The reaction mixture is stirred for two hours at ambient temperature. The white solid obtained after filtration is washed with water (in order to eliminate the excess of HBF_4) then twice with 30 ml of ether and finally dried under vacuum.

White solid **Yield** = 98% **Mp** = 154-156°C

^{1}H NMR (200 MHz, Acetone D_6): 2.39-2.57 (m, 2H); 3.35 (s, 9H); 3.70-3.87 (m, 2H); 4.50 (t, 2H,J = 5.91 Hz), 7.73 (dd, 2H, J_1 = 1.97 Hz; J_2 = 6.77 Hz); 8.02 (dd, 2H, J_1 = 1.77 Hz; J_2 = 6.47 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 22.96; 53.14 (4.1 Hz); 62.35; 64.29; 128.01; 129.52; 131.85; 132.24; 165.61

^{19}F NMR (282 MHz, Acetone D_6): -150.16(s, B-F)

Mass spectrometry (FAB) for $C_{26}H_{38}F_4N_2O_4Br_2B$

Theoretical mass calculated for ($2C^+$, $BF4^-$)	689.1228
Mass found	689.1234

* 7e:

1.5 eq of DCC, 1.5 eq of 4-vinylbenzoic acid are added to a mixture of the alcohol **1b** in 100 ml of CH_3CN, in the presence of 0.02 eq of DMAP. The reaction mixture is stirred for 4 hours at ambient temperature then evaporated to dryness. The ester formed is extracted with 3 × 30 ml of water. 1.5 eq of $NaBF_4$ in solution in water is added to this solution.. The reaction mixture is stirred for two hours at ambient temperature. The white solid obtained after filtration is washed with water (in order to eliminate the excess of $NaBF_4$) then twice with 30 ml of ether and finally dried under vacuum.

Appearance of the product: white solid **Yield** = 75 % **Mp** = 138-140°C

^{1}H NMR (300 MHz, Acetone D_6): 2.30-2.48 (m, 2H); 3.38 (S, 9H); 3.69-3.82 (m, 2H); 4.36 (t, 2H, J=6.0 Hz), 6.58 (d, 1H, J=16.1Hz); 7.40-7.50 (m, 3H); 7.63-7.78 (m, 3H).

^{13}C NMR (75MHz, Acetone D_6): 22.68; 52.79 (t, J= 3.8 Hz); 60.88; 63.86 (t, J= 3.32Hz); 117.76; 128.20; 128.95; 130.43; 134.42; 144.86; 165.99.

Mass spectrometry (APCI) for [$C_{15}H_{22}NO_2$][BF_4]

Theoretical mass calculated for (C^+)	248.3
Mass found	248.2

* 7f:

Method 1

5 ml of thionyl chloride (68.54 mmol) is added, dropwise and at 0°C, to a solution of 5 g (36.46 mmol) 4-aminobenzoic acid in 30 ml of 3-chloropropanol. The reaction mixture is then taken to 100°C for 3 hours. 50 ml of ether is then added and the white solid thus formed is filtered then washed with 3 × 10 ml of ether. The solid is then dissolved in 30 ml of water and the ester is then extracted with 3 × 20 ml of ethyl acetate. The organic phase is finally washed with 20 ml of a saturated solution of K_2CO_3 and evaporated.

The mixture constituted by the white solid obtained, 5 ml of a solution of trimethylamine at 45% in water and 0.5g of NaI are dissolved in 20 ml of acetonitrile. They are then taken to reflux for 16 hours. After this the solvent is evaporated off and the product is crystallized from acetone.

White solid Yield (in two stages)= 58% Pf= 120-122°C

Method 2

1.5 eq of DCC 1.5 eq of 4-nitrobenzoic acid in the presence of 0.02 eq of DMAP is added to the alcohol mixture **1b** in 100 ml of CH_3CN. The reaction mixture is stirred for 4 hours at ambient temperature then evaporated to dryness and the ester formed is extracted with 3 × 30 ml of water. Reduction of the nitro group is carried out by adding to this solution 0.01 eq of Pd/C 5% under stirring at ambient temperature under a pressure of 5 bar hydrogen for 8 hours. After filtration and evaporation of the water the product is recrystallized from acetone.

Yield= 90%

^{1}H NMR (200 MHz, D_2O): 2.1-2.25 (m, 2H); 3.09 (s, 9H); 3.32-3.45 (m, 2H); 4.48 (t, 2H, J = 6.15 Hz); 6.75 (d, 2H, J = 7.78 Hz); 7.72 (d, 2H, J = 7.78 Hz).

^{13}C NMR (50 MHz, D_2O): 22.61; 30.63; 53.37 (t, J_{C-N} = 4.1 Hz); 61.88; 64.23; 114.91; 118.20; 132.02; 153.03; 168.80

*** 7g:**

4.77 mmol of $LiNTf_2$ in solution in water is added to a solution of 1 g (3.67 mmol) of 7f in 10 ml of water. After stirring at ambient temperature for 2 hours, the white solid obtained is filtered then dried.

White solid Yield = 93% Mp = 109-110°C

^{1}H NMR (200 MHz, Acetone D_6): 2.35-2.51 (m, 2H); 3.41 (s, 9H); 3.78-3.92 (m, 2H); 4.5 (t, 2H, J = 6.1 Hz); 5.51 (signal large, 2H); 6.58 (d, 2H, J = 7.9 Hz); 7.84 (d, 2H, J_1 = 7.7 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 24.17; 29.12; 54.12 (t, J_{C-N} = 4.1 Hz); 61.72; 65.60; 114.25; 118.33; 121.17 (q, J_{C-F} = 320.9 Hz); 132.72; 154.74; 167.08

*** 7h:**

1.5 eq of DCC, 1.5 eq of 4-carboxybenzaldehyde and 0.2 eq of DMAP is added to a mixture of the alcohol 1b in 100 ml of CH_3CN. The reaction mixture is stirred for 4 hours at ambient temperature then evaporated to dryness. The ester formed is extracted with 3 × 30 ml of water. 1.5 eq of 50% HBF_4 in solution in water is added to this solution of the ester in water. The reaction mixture is stirred for two hours at ambient temperature. The yellow solid obtained after filtration is washed with water (in order to

eliminate the excess of HBF_4) then twice with 30 ml of ether and finally dried under vacuum.

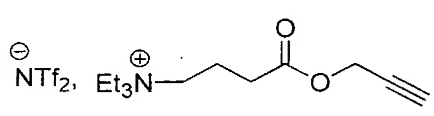
Appearance of the product: yellow solid **Yield** = 90% **Mp** = 146-148°C

^{1}H NMR (200 MHz, CD_3CN): 2.10-2.33 (m, 2H); 3.05 (s, 9H); 3.36-3.55 (m, 2H); 4.45 (t, 2H, J=5.8 Hz), 8.00 (dd, 2H, J_1=1.6Hz, J_2=6.6Hz); 8.13 (dd, 2H, J_1=1.4Hz, J_2=8.3 Hz); 10.10 (s, 1H).

^{13}C NMR (50MHz, CD_3CN): 22.08; 52.66 (t, J= 3.8Hz); 61.53; 63.52 (t, J= 3.02Hz); 129.10; 129.80; 134.39; 139.27; 164.89; 192.04.

Mass spectrometry (APCI) for [C_{14} $H_{20}NO_3$][BF_4]	
Theoretical mass calculated for (C^+)	250.3
Mass found	250.2

4/ Supported alkyne:

<u>**8**</u>	

0.9 eq of 4-chlorobutyryl chloride at 0°C are added dropwise to a solution of 25 mmol of propargylic alcohol in 25 ml of anhydrous methylene chloride and 5 eq of Et_3N. The reaction mixture is stirred for 3 hours at temperature, evaporated to dryness and the ester formed is isolated after extraction with 3 × 10 ml of ether followed by distillation in a ball oven (60°C, 0.2 mmHg). The salt obtained after the quaternization reaction at 80°C in the presence of triethylamine, acetonitrile and NaI is used in the metathesis reaction in water in the presence of $LiNTf_2$, to produce the product <u>8</u>.

Appearance of the product: orange oil Yield = 85 %

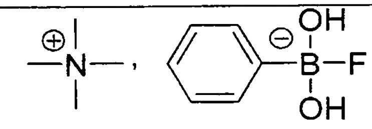
^{1}H NMR (200 MHz, Acetone D_6): 1.36-1.55 (m, 9H); 2.05-2.30 (m, 2H); 2.65 (t, J=6.7 Hz, 2H); 3.05-3.15 (m, 1H); 3.39-3.68 (m, 8H); 4.76 (d, J=2.5Hz, 2H).

^{13}C NMR (50 MHz, Acetone D_6)**:** 7.13; 17.20; 52.19; 53.19 (t, J=2.8Hz); 56.07; 120.46 (q, J_{CF}=321.4 Hz); 171.68.

Mass spectrometry (APCI) for [C_{13} H_{24}NO2][$C_2NS_2O_4F_6$]

Theoretical mass calculated for (C^+)	226.3
Mass found	226.4

III) ONIUM SALTS WITH FUNCTIONALIZED ANION:

9	

0.1 g (2.1 mmol) of anhydrous tetramethylammonium fluoride is introduced into a 10 mL single-necked flask. Then 1 mL of anhydrous THF is added and the solution is homogenized while heating if necessary. Finally, 0.13 g of phenylboronic acid (2.1 mmol) is introduced. Stirring is continued for approximately 2 hours at ambient temperature.

After stirring for 2 hours, anhydrous ether is added, then the solid is filtered on sintered glass. The solid is washed 2 or 3 times with 20 ml of ether and finally, it is placed under vacuum to dry.

White solid **Yield**= 82% **Mp** = 162-164°C

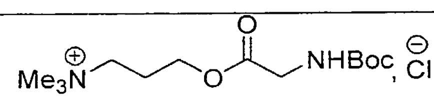
***^{1}H NMR (200 MHz, Acetone D_6)*:** 3.15 (s, 12H); 6.8-7.4 (m, 3H); 7.50-7.70 (m, 2H)

^{13}C NMR (50 MHz, Acetone. D_6): 56.19 (t, J_{C-N} = 3.97 Hz); 127.47; 128.36; 130.91; 132.98; 135.96

^{19}F NMR spectrum (300 MHz, Acetone. D_6): -136.40 (multiplet)

^{11}B NMR spectrum (300 MHz, Acetone. D_6): 4.66 (D, J_{B-F} = 27.4 Hz) (56%); 28.5 (44%)

IV) GLYCINE DERIVED ESTERS:

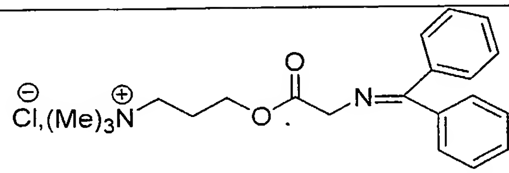
10	

2.0 g (11.3 mmol) of N-Boc-glycine and 1.6 g of **1b** (11.2 mmol) are dissolved in 15 ml of methylene chloride and 11.2 mmol of DCC and 5 molar % DMAP are added. The mixture is stirred at ambient temperature for 18 hours. After filtration of the precipitate formed during the course of the reaction, the filtrate is evaporated to dryness and the product obtained is washed with 5 × 20 ml of ether then dried under vacuum.

Colourless oil **Yield = 92%**

^{1}H NMR (200 MHz, D_2O): 1.39 (s, 9H); 2.4-2.5 (m, 2H); 3.08 (s, 9H); 3.35-3.45 (m, 2H); 3.75 (s, 2H); 3.32 (t, 2H, J = 6.9Hz)

^{13}C NMR (50 MHz, D_2O): 23.82; 39.07; 47.31; 53.69 (t, J_{C-N} = 4.0 Hz); 61.62; 65.33; 166.92; 178.06

11	

Hydrochloric acid is bubbled through a solution of the ester **10** in 15 ml of methylene chloride for 6 hours. The white precipitate which forms after stirring at ambient temperature for 24 hours is washed twice with ether. The product thus obtained is added to a solution of diphenylmethylene imine (2.0 g; 11 mmol) in 15 ml of methylene chloride. The reaction mixture is then stirred at ambient temperature for 24 hours. The precipitate formed is filtered, the solvent evaporated off, followed by washing with 3 × 10 ml of ether.

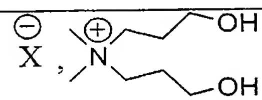
Yield in 2 stages: 62%

***^{1}H NMR (200 MHz,D_2O)*:** 2.49-2.52 (m, 2H); 3.18 (s, 9H); 3.43-3.49 (m, 2H); 4.19 (s, 2H); 4.31 (t, 2H, J = 6.9 Hz); 7.18-7.67 (m, 8H); 7.82 (m, 2H)

***^{13}C NMR (50 MHz, D_2O)*:** 23.89; 54.03; 55.14 (t, $J_{C\text{-}N}$ = 4.0 Hz); 61.98; 65.74; 127.98; 128.33; 128.94; 129.19; 130.67; 130.93; 140.03; 167.68; 177.38

V) BIFUNCTIONAL ONIUM SALTS:

1/ Synthesis of the salts 12:

12	

12a	**X = Cl**
12b	**X = NTf_2**

* **12a:**

30 ml of acetonitrile is mixed with a 45% solution of 4.5g of dimethylamine (0.1 mole) in water. 17 g of K_2CO_3, 150 mg of NaI and 25 ml (0.3 mol) of chloropropanol are added. The reaction mixture is heated to 70°C overnight. After evaporation of the acetonitrile the salt is extracted with 3 × 10 ml of methanol and it is then crystallized from acetone.

White solid **Yield** = 87% **Mp**=112-114°C

^{1}H NMR (200 MHz, D_2O): 1.7-1.85 (m, 4H); 2.85 (s, 6H); 3.05-3.2 (m, 4H); 3.4 (t, 4H, J = 6.1 Hz)

^{13}C NMR (50 MHz, D_2O): 25.25; 51.10 (t, $J_{C\text{-}N}$ = 4.1 Hz); 58.94; 62.01 (t, $J_{C\text{-}N}$ = 4.0 Hz)

Mass spectrometry (FAB) for $C_{16}H_{40}N_2O_4Cl$

Theoretical mass calculated for ($2C^{+}\cdot Cl^{-}$)	359.2677
Mass found	359.2675

* **<u>12b</u>:**

A solution of 5.0 g (25.30 mmol) of **<u>12a</u>** in 10 ml of distilled water is introduced into a 100 ml flask. A solution of 10 g (32.89 mmol) of $LiNTf_2$ in water is added to this solution.

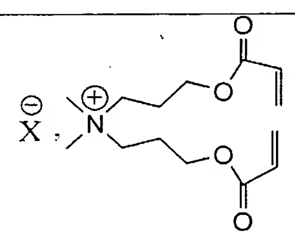
After stirring for 2 hours at ambient temperature the water is evaporated and the product is extracted with 3 × 10 ml of acetone.

Colourless oil Yield = 90%

^{1}H NMR (200 MHz, D_2O): 1.82-2.05 (m, 4H); 3 (s, 6H); 3.25-3.40 (m, 4H); 3.46(t, 4H, J = 6.9 Hz)

^{13}C NMR (50 MHz, D_2O): 25.34; 51.09; 58.53; 62.13; 121.05 (q, J = 321.2 Hz)

2/ Diester synthesis <u>13</u>:

<u>13</u>	

* **X = NTf_2**

A solution of 2.7 g (6.02 mmol) of **<u>12b</u>** and 6 equivalents of acryloyl chloride in acetonitrile is heated to 80°C in the presence of 10 equivalents of solid K_2CO_3 for 2 hours. The mixture is then placed under vacuum at 40°C in order to eliminate the solvent and the excess of the reagent. The ammonium acrylate thus obtained by dichloromethane extraction is stable at 4°C and can be stored for several months.

Pale yellow oil **Yield** = 87 %

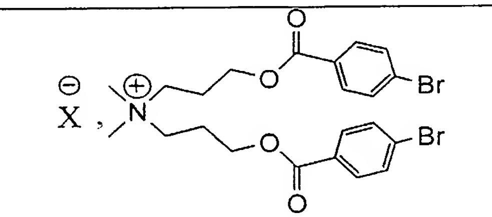
^{1}H NMR (200 MHz, Acetone D_6): 2.3-2.5 (m, 4H); 3.42 (s, 6H); 3.72-3.82 (m, 4H); 4.32 (t, 2H, J= 5.8 Hz); 5.95 (dd, 2H, J_1 = 1.8; J_2 = 10.1); 6.18 (dd, 2H, J_1 = 10.1 Hz; J_2 = 17.1 Hz); 6.4 (dd, 2H, J_1 = 2.1 Hz; J_2 = 17.1 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 22.52; 51.14; 61.89; 61.95; 121.05 (q, J=321.2Hz); 128.78; 131.02; 165.81

Mass spectrometry (FAB) for $C_{14}H_{24}O_4N$

Theoretical mass calculated for (C^+)	270.1750
Mass found	270.1703

2/ Diester synthesis <u>14</u>:

<u>14</u>	

<u>14a</u>	**X = Cl**
<u>14b</u>	**X = BF_4**

*** <u>14a</u>:**

1 g (5.06 mmol) of **<u>12a</u>** chloride, 10 ml of acetonitrile, 4.3 g of K_2CO_3 in powder form and 4.2 g (19.14 mmol) of 4-bromobenzoic acid chloride are introduced into a 100 ml flask. After stirring overnight at ambient temperature, the K_2CO_3 is filtered and washed with 3 times 15 ml of methylene chloride and finally evaporated to dryness. This is taken up in water and the excess of the 4-bromobenzoic acid, which crystallizes by filtration, is eliminated. The product is then crystallized from acetone after evaporation of the water.

White solid **Yield** = 60% **Mp**= 112-114°C

^{1}H NMR (200 MHz, MeOH-d_4): 2.05-2.25 (m, 4H); 3.1 (s, 6H); 3.35-3.53 (m, 4H); 4.21 (t, 4H, J = 5.8 Hz); 7.1 (d, 4H, J = 8.6 Hz); 7.35 (d, 4H, J_1 = 8.6 Hz).

^{13}C NMR (50 MHz, MeOH-d_4): 23.87; 52.50; 62.50; 63.64; 130.08; 130.16; 132.78; 133.63; 168.22

Mass spectrometry (FAB) for $C_{22}H_{26}NO_4Br_2$

Theoretical mass calculated for (C^+)	526.0229
Mass found	526.0221

* **<u>14b</u>:**

0.2 ml of 40% HBF_4 in solution in water is added to a solution of 100 mg (0.18 mmol) of **<u>14a</u>** in 5 ml of water. After the former has been added, formation of a white solid is noted. The reaction mixture is stirred for two hours at ambient temperature. The white solid obtained after filtration is washed with water (in order to eliminate the excess of HBF_4) then twice with 30 ml of ether and finally dried under vacuum.

White solid **Yield** = 80% **Mp**= 172-174°C

^{1}H NMR (200 MHz, Acetone D_6): 2.4-2.57 (m, 4H); 3.4 (s, 6H); 3.8-3.94 (m, 4H); 4.45 (t, 4H, J = 5.8 Hz); 7.67 (d, 4H, J = 8.6 Hz); 7.95 (d, 4H, J_1 = 8.6 Hz)

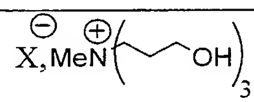
^{13}C NMR (50 MHz, Acetone D_6): 23.55; 51.99 (t, J = 4.1 Hz); 62.81; 63.12; 128.92; 130.41; 132.65; 133.14; 166.36

Mass spectrometry (FAB) for $C_{22}H_{26}NO_4Br_2$

Theoretical mass calculated for (C^+)	526.0229
Mass found	526.0216

VI) TRI- AND TETRAFUNCTIONAL ONIUM SALTS HAVING IDENTICAL FUNCTIONS:

1/ Trifunctional salts <u>15</u>:

<u>15</u>	

<u>15a</u>	**X = Cl**
<u>15b</u>	**X = NTf_2**

* **<u>15a</u>:**

3 ml (87.15 mmol) of methylamine, 20 ml of acetonitrile, 12 g of K_2CO_3, 53 mg of NaI and 12 ml of 3-chloropropanol are introduced into a Schlenk tube. The reaction mixture is heated to 80°C for 48 hours. After evaporation of the solvent the salt is extracted with 3 × 10 ml of methanol. It is then crystallized from acetone after evaporation of the solvent.

White solid **Yield** = 75% **Mp**> 260°C

^{1}H NMR (200 MHz, D_2O): 1.8-2.03 (m, 6H); 3.1 (s, 3H); 3.25-3.4 (m, 6H); 3.4 (t, 6H, J = 5.8 Hz)

^{13}C NMR (50 MHz, D_2O): 24.89; 48.6; 58.47; 59.60

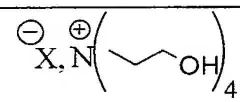
* **15b:**

A solution of 0.4 g (1.65 mmol) of **15a** in 1 ml of distilled water is introduced into a 100 ml flask. A solution of 0.7 g (2.14 mmol) of $LiNTf_2$ in water is added to this solution. After stirring at ambient temperature for 2 hours, the water is evaporated and extracted **14b** with 3 × 10 ml of acetone. After evaporation of the solvent and drying under vacuum, 0.64 g of a colourless oil is obtained, i.e. a yield of 80%.

^{1}H NMR (200 MHz, MeOH-d_4): 1.92-2.01 (m, 6H); 3.1 (s, 3H); 3.38-3.52 (m, 6H); 3.7 (t, 6H, J = 5.5 Hz)

^{13}C NMR (50 MHz, MeOH-d_4): 25.25; 29.92; 58.35; 59.80; 121.05 (q, J = 321.2 Hz)

2/ Tetrafunctional salts 16:

16	

16a	**X = Cl**
16b	**X = NTf_2**

* **16a:**

1 g (5.23 mmol) of propanolamine and 2 ml (23.90 mmol) of 3-chloro-1-propanol are introduced into a 100 ml flask. After heating the reaction mixture overnight at 150°C, the excess of chloropropanol is eliminated by washing with ether (3 × 10 ml). The product is thus isolated by filtration after crystallization from acetone.

White solid **Yield** = 58%

^{1}H NMR (200 MHz, D_2O): 2-2.2 (m, 8H); 3.4-3.6 (m, 8H); 3.8(t, 8H, J = 5.7 Hz)

^{13}C NMR (50 MHz, D_2O): 24.49; 56.56; 58.40

* **16b**:

A solution of 1 g (3.5 mmol) of **16a** in 5 ml of distilled water is introduced into a 100 ml flask. A solution of 2 g (4.55 mmol) of $LiNTf_2$ in water is added to this solution. After stirring at ambient temperature for 2 hours the water is evaporated and **15b** is extracted with 3 × 5 ml of methanol. After evaporation of the solvent and drying under vacuum, a colourless oil is obtained.

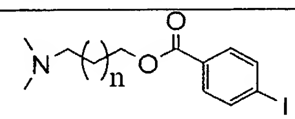
Colourless oil **Yield**= 85%,

NMR ^1H (200 MHz, D_2O): 1.7-1.93 (m, 8H); 3.15-3.30 (m, 8H); 3.58 (t, 8H, J = 5.8 Hz)

NMR ^{13}C (50 MHz, D_2O): 24.56; 56.67; 58.38; 121.05 (q, J = 321.2 Hz)

VII) SYNTHESIS OF THE MULTIFUNCTIONAL ONIUM SALTS HAVING DIFFERENT FUNCTIONS:

1/ Preparation of the precursor tertiary amines 17:

17	

17a	n = 1
17b	n = 2

* **17a**:

1 g (9.7 mmol) of 1-dimethylamino-3-propanol, 10 ml of anhydrous methylene chloride, 3 g of K_2CO_3 and 2.84 (10.66 mmol) of chloride derived from 4-iodobenzoic acid are introduced into a 100 ml flask. After stirring at ambient temperature for 3 hours the reaction is complete. The reaction mixture is then filtered and evaporated to dryness. A white solid is obtained with a yield of 90% (Mp = 48-50°C).

^1H NMR (200 MHz, $CDCl_3$): 1.87-2.03 (m, 2H); 2.3(s, 6H); 2.45 (t, 2H, J = 7.0 Hz); 4 (t, 2H, J = 6.5 Hz); 7.3-7.5 (m, 4H)

^{13}C NMR (50 MHz $CDCl_3$): 27.36; 45.85; 56.58; 63.96; 101.15; 130.17; 131.37; 138.04; 166.34

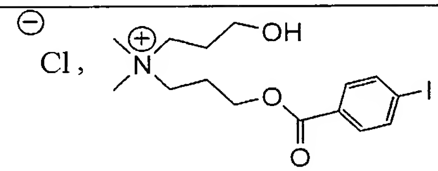
* **<u>17b</u>:**

2.8 g (23.93 mmol) of 1-N,N'-dimethylamino-4-butanol, 10 ml of anhydrous methylene chloride, 6.6 g of K_2CO_3 and 7.0 g (26.27 mmol) of acid chloride are introduced into a 100 ml flask. The reaction is exothermic. After stirring at ambient temperature for 3 hours the reaction is complete. The reaction mixture is then filtered and evaporated to dryness in order to produce a white solid, with a yield of 88%.

^{1}H NMR (200 MHz, $CDCl_3$): 1.78-1.9 (m, 4H); 2.5(s, 6H); 2.65 (t, 2H, J = 5.3 Hz); 4.35 (t, 2H, J = 6.0 Hz); 7.7-7.85 (m, 4H)

^{13}C NMR (50 MHz $CDCl_3$): 20.25; 24.86; 43.51; 57.34; 63.47; 98.97; 128.39; 129.39; 136.16; 164.26

2/ Synthesis of the salts <u>18</u>:

<u>18</u>	

<u>18a</u>	**X = Cl**
<u>18b</u>	**X = NTf_2**

* **<u>18a</u>:**

1.0g (3 mmol) of **<u>17a</u>** and 0.5 ml of 3-chloro-1-propanol are introduced into a 50 ml flask. After 30 minutes of heating of the reaction mixture at 110°C, the formation of a white solid is observed. The latter is isolated by filtration after crystallization from acetone and washing with 3 × 10 ml of ether.

White solid **Yield** = 94% **Mp** = 180-182°C.

^{1}H NMR (200 MHz, D_2O): 1.8-2 (m, 2H); 2.10-2.30(m, 2H); 3.05 (s, 6H); 3.25-3.45(m, 4H); 3.6 (t, 1H, J = 0.7 Hz); 4.35(t, 2H, J = 0.7 Hz); 7.85 (d, 2H, J = 8.1 Hz); 8 (d, 2H, J= 8.1 Hz)

^{13}C NMR (50 MHz, D_2O): 22.18; 25.29; 51.27 (t, J = 4.3 Hz); 58.42; 62.00; 101.85; 129.94; 131.13; 138.26; 165.49

Mass spectrometry (FAB) for $C_{15}H_{23}NO_3I$

Theoretical mass calculated for (C^+)	392.0723
Mass found	392.0720

* **18b:**

A solution of 1.0 g (2.34 mmol) of **18a** in 5 ml of distilled water is introduced into a 100 ml flask. A solution of 3.04 mmol of $LiNTf_2$ in water is added to this solution. After stirring at ambient temperature for 2 hours **18b** is extracted with 3 × 5 ml of methylene chloride which is then driven off under vacuum in order to produce a white solid.

White solid **Yield** = 91% **Mp** = 90-92°C

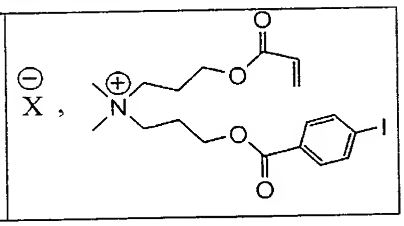
^{1}H NMR (200 MHz, Acetone D_6): 2.12-2.63 (m, 2H);2.45-2.63(m, 2H) 3.4 (s, 6H); 3.7-3.93 (m, 6H); 4.1 (t, 1H, J = 0.3 Hz), 4.55 (t, 2H,J = 0.7 Hz); 7.85 (d, 2H, J = 8.1 Hz); 8 (d, 2H, J = 8.1 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 22.62; 26.03; 51.16 (t, J = 4.3 Hz); 58.56; 62.21; 100.96; 121.01 (q; J_{CF3} = 321.0 Hz); 129.94; 131.51; 138.33; 165.79.

Mass spectrometry (FAB) for $C_{32}H_{46}N_3O_{10}F_6I_2S_2$

Theoretical mass calculated for ($2C^+$, $NTf2^-$)	1064.0618
Mass found	1064.0607

3/ Synthesis of the salts with different functionalities 19:

19	

19a	**X = Cl**
19b	**X = NTf_2**

A solution of 1 mmol of **18a** or **18b** and 3 equivalents of acryloyl chloride in acetonitrile is heated at 80°C in the presence of 5 equivalents of solid K_2CO_3 for 2 hours. The mixture is then filtered and evaporated under vacuum at 40°C. The ammonium ester is then extracted with methylene chloride and stored at 4°C after evaporation of the solvent.

19a: White solid **Yield** =75 %.

^{1}H NMR (200 MHz, D_2O): 2.05- 2.32 (m, 4H); 3.1 (s, 6H); 3.35-3.55 (m, 2H); 4.18 (t, 2H, J = 5.5 Hz); 4.35 (t, 2H, J = 5.8 Hz) 5.90 (dd, 1H, J_1 = 1.9 Hz; J_2 = 10.7);

6.05 (dd, 1H, J_1 = 17.2 Hz; J_2 = 10.7 Hz); 6.3 (dd, 1H, J_1 = 1.9 Hz; J_2 = 17.2 Hz); 7.62 (d, 2H, J = 8.6 Hz); 7.82 (d, 2H, J = 7.8 Hz)

^{13}C NMR (50 MHz, D_2O): 22.09; 22.86; 51.39 (t, J = 4.2 Hz); 62.13; 62.65; 63.03; 63.35; 101.78; 127.53; 128.92; 131.13; 133.05; 139.63; 168.07; 168.45

Mass spectrometry (FAB) for $C_{18}H_{25}NO_4I$

Theoretical mass calculated for (C^+)	426.0828
Mass found	446.0821

<u>19b</u>:

A solution of 1.0 g (1.80 mmol) of **<u>19a</u>** in 5 ml of distilled water is introduced into a 100 ml flask. A solution of 2 mmol of $LiNTf_2$ in solution in water is added to this solution. After stirring at ambient temperature for 2 hours **<u>19b</u>** is extracted with 3 × 5 ml of methylene chloride. After elimination of the solvent under vacuum, a colourless oil is obtained. **Yield**= 78%

^1H NMR (200 MHz, Acetone D_6): 2.31-2.65 (m, 4H); 3.5 (s, 6H); 3.75-3.93 (m, 4H); 4.32 (t, 2H, J = 6.0 Hz), 4.55 (t, 2H, J = 6.1 Hz); 5.95 (dd, 1H, J_1 = 1.9 Hz, J_2 = 10.3 Hz); 6.2 (dd; 1H; J_1 = 17.2 Hz; J_2 =10.3 Hz); 6.43 (dd; 1H; J_1 =1.9 Hz; J_2 = 17.2 Hz); 7.82 (d, 2H, J = 8.1 Hz); 7.78(d, 2H, J = 8.1 Hz)

^{13}C NMR (50 MHz, Acetone D_6): 23.49; 23.54; 52.12 (t, J = 4.31 Hz); 62.16; 62.89; 100.84; 121.09 (q, J_{CF3} = 321 Hz); 124.56; 129.38; 130.82; 132.22; 132.38; 139.23; 166.66.

<u>34i</u>:

4 eq of phenylacetylene and 5 molar % CuI are added to a solution of 1g (1.55 mmol) of <u>6b</u> in 10 ml of the CH_3CN/NEt_3 mixture (2/1). The reaction mixture is stirred for 5 minutes at ambient temperature before adding 2.5% $PdCl_2$ $(PPh_3)_2$.

After 15 minutes of stirring at ambient temperature, the reaction mixture is evaporated to dryness and washed with ether in order to eliminate the excess of reagents. The oil thus obtained is dissolved in methylene chloride and then washed with a diluted solution of K_2CO_3 in water to release Et_3N from its hydrochloride formed during the reaction. After treatment with Na_2SO_4 and evaporation of the methylene chloride, the product is isolated by filtration after cystallization from ether and drying under vacuum.

Appearance of the product: white solid Yield = 87% Mp = 228-230°C

^{1}H NMR (CD3CN, 300Mhz): 1.72-1.93 (m, 4H); 3.05 (s, 9H); 3.23-3.40 (m, 2H); 4.38 (t, J=6.1 Hz, 2H); 7.38-7.45 (m, 3H); 7.55-7.64 (m, 2H); 7.70 (dd, J=8.5 Hz, 2H); 8.10 (dd, J=8.5 Hz, 2H).

^{13}C NMR (CD3CN, 75Mhz): 19.17; 24.70; 52.61 (t, J=3.8 Hz); 63.86; 65.65 (t, J=3.0 Hz); 87.93; 91.93; 124.63 (q, J_{CF}=412 Hz); 128.42; 128.85; 129.24; 129.44; 131.20; 131.24; 165.63.

Mass spectrometry (APCI) for $[C_{22}H_{26}NO_2][C_2NS_2O_4F_6]^-$

Theoretical mass calculated for (C^+)	336.4
Mass found	336.0

Uses in synthesis – General protocol of the different reactions:

1/ Diels-Alder reaction:

a- For cyclopentadiene:

A solution of the supported acrylic ester (from mono to tetra-functionalized) and 10 equivalents of cyclopentadiene in 2 ml of methylene chloride is stirred for two hours at ambient temperature. The excess of the reagent and the solvent are then eliminated under vacuum. The reaction product thus obtained is placed in solution in methanol in the presence of three drops of hydrochloric acid 12 N. After twelve hours at reflux, the transesterification is complete and the product is then extracted with pentane after evaporation of the alcohol under vacuum. The pentane is then eliminated under vacuum in order to produce pure methyl esters.

b- For the various other dienes:

0.01 eq of hydroquinone and 5 eq of dienes are added to a solution of 5a in acetonitrile. The reaction mixture is heated to 120°C in sealed tubes, evaporated to dryness then washed with ether. The reaction product thus obtained is placed in solution in methanol in the presence of a catalytic quantity of 12 N hydrochloric acid. After twelve hours at reflux, the product is then extracted with ether after evaporation of the alcohol under vacuum. The ether is then eliminated under vacuum in order to produce the pure methyl esters.

2/ Heck reaction:

a- With supported acrylic ester 5:

1.5 mmol of supported substrate are dissolved in 2 ml of solvent. 5 equivalents of aryl halide, 1 equivalent of K_2CO_3 as base and 1molar % palladium acetate are added to this solution. At the end of the reaction the solvent and the excess of the reagent are eliminated by washing with ether then methanol (2ml) and 12 N hydrochloric acid (3 drops) are added and the solution is taken to reflux.

After 12 hours, the coupling product is extracted with ether after evaporation of the alcohol. The ether solution is then evaporated to dryness leading to the expected product.

b- With supported iodoaryl ester 6g:

0.5 mmol of supported substrate 6g is dissolved in 1 ml of DMF. 5 eq of olefin (tertiobutyl acrylate, dimethylacrylamide or styrene), 1.5 eq of K_2CO_3 as base and 1 to 5 molar % palladium acetate are added to this solution. At the end of the reaction, the solvent and the excess of the reagent are eliminated by washing with ether then methanol (2 ml) and 12 N hydrochloric acid (3 drops) are added and the solution is taken to reflux.

After 12 hours, the coupling product is extracted with ether after evaporation of the alcohol and neutralization of the medium by the addition of a diluted solution of K_2CO_3 in water. The ether solution is then evaporated to dryness.

c- With supported styrene 7e:

1 ml of NEt_3 (3 eq), 27 mg of $Pd(OAc)_2$ (0.05 eq) and 0.125 eq of each iodide used are added to a solution of 800 mg (2.38 mmol) of 7e in 3 ml of DMF. After heating at 110°C for two hours, the oil thus obtained after the addition of the ether is transesterified in the presence of methanol and a few drops of hydrochloric acid.

3/ Suzuki coupling reaction:

General procedure for the mono and bifunctionalized salts:

0.95 equivalents of boronic acid (per function), 2 equivalents of K_2CO_3 and 1 molar % palladium acetate are added to a solution of 100 mg of supported aryl halide in 1 ml of DMF. The reaction mixture is heated for 5 hours at 80°C. After which, an alcohol is added and the mixture is taken to reflux for 12 hours, in the presence of 0.1 ml of concentrated hydrochloric acid (12 N). After transesterification and evaporation

of the alcohol, the ester formed is extracted from the medium by washing with ether (3 × 10 ml).

4/ Sonogashira coupling reaction:

a- For supported iodoaryl ester:

4 equivalents of alkyne, 1 equivalent of K_2CO_3 and a mixture (1/2 catalyst/CuI) are added to a solution of 100 mg of supported aryl halide in 1 ml of solvent. The reaction mixture is heated for 1 hour at 40°C, after which an alcohol is added and the mixture is taken to reflux for 12 hours, in the presence of 0.1 ml of concentrated hydrochloric acid (12 N). After transesterification and evaporation of the alcohol, the ester formed is extracted from the medium by washing with ether (3 × 10 ml) and isolated after evaporation of the ether.

b- For the supported alkyne:

4 eq of aryl iodide and 0.2 eq of CuI are added to a solution of 100 mg of supported alkyne 8 in 1 ml of the CH_3CN/NEt_3 mixture (2/1). The reaction mixture is stirred for 5 minutes before addition of 0.1 eq of $PdCl_2(PPh_3)_2$. After reaction, the alcohols formed are extracted with ether after evaporation of the solvent and elimination of the excess of the reagents followed by a saponification reaction in the presence of 5 ml of NaOH(2N).

5/ Alkylation of the supported Schiff's base:

The halogenated derivative RX (4 mmol) is added at ambient temperature to a mixture of the supported Schiff's base **11** (1g; 2.6mmol) and 2 equivalents of K_2CO_3 in acetonitrile (2 ml). The mixture is then taken to reflux under vigorous stirring. After 12 hours, the reaction medium is filtered then evaporated to dryness.

The transesterification and the hydrolysis of the imine are carried out at reflux of the methanol in the presence of concentrated hydrochloric acid for 12 hours. After evaporation of the solvent the mixture is dissolved in 1 ml of water. The free amino acid is extracted with methanylene chloride after neutralization of the medium.

6/ Multi-component reaction of the Grieco type:

100 mg of supported amine **34**, 500 µl of a 1 M solution of aldehyde in acetonitrile, 500 µl of a 1 M solution of cyclopentadiene in acetonitrile and 50 µl of a 1% TFA solution in acetonitrile are mixed under a flow of argon. The reaction mixture

is stirred overnight at ambient temperature. After evaporation to dryness and washing with ether, a solid is obtained.

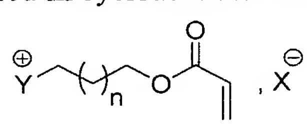
7/ Synthesis of the tetrasubstituted olefins:

2 eq of iodide, 3 eq of boronic acid and 1.2 mg of $PdCl_2(PPh_3)_2$ (0.01 eq) are added to a solution of 100 mg (0.16 mmol) of 34i in 0.5 ml of the DMF/H_2O mixture. After heating at 100°C for three hours, the orange oil obtained after addition of ether is dissolved in 10 ml of methylene chloride and washed with 2 × 3 ml of H_2O. After treatment of the aqueous phase with $MgSO_4$ and evaporation to dryness, the tetrasubstituted olefins are isolated by filtration after crystallization from ether.

EXAMPLES

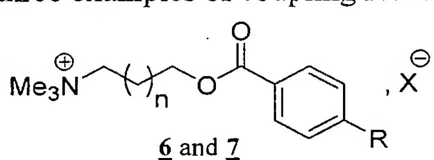
In order to show the advantage of the ammonium salts as novel soluble supports, the reagents **5**, **6**, **7** and **11** allowing the use of several types of fundamental reactions in organic chemistry were chosen:

– acryl esters 5 were used in cycloaddition and coupling reactions



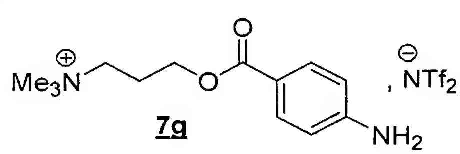
5

– an aryl ester substituted by an R (Br ,I, or CH2=CH) on the aromatic ring which was tested in three examples of coupling reactions.



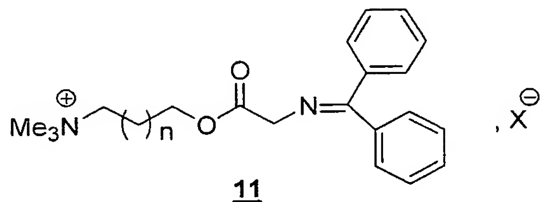
6 and 7

– an aryl ester substituted by an R = NH_2 on the aromatic ring which was tested in the Grieco reaction.



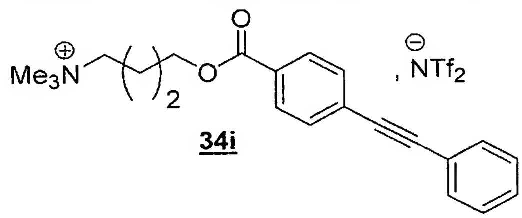
7g

– the Schiff's base derived from glycine which, after alkylation, will lead to higher amino acids



11

– an aryl ester substituted by an R = PhC≡CH on the aromatic ring which was tested in the synthesis of the tetrasubstituted olefins.



34i

In order to increase the specific charge of the onium salts, the present inventors have also developed novel onium salts having more than one functionalized arm.

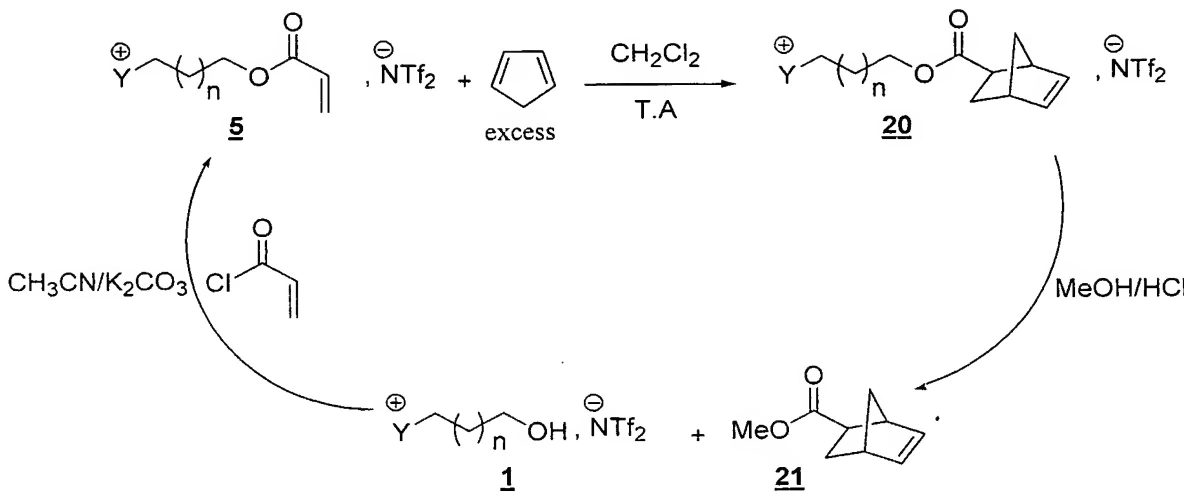
The synthesis of supports and supported reagents as well as their applications in a few examples is described in detail in the following experimental part.

A - Example 1: Diels-Alder Reaction:

1) Reaction with cyclopentadiene.

The richness and the synthetic potential of the Diels-Alder reaction have led chemists to research methods on the one hand allowing an increase of their speed and yield and on the other hand of their regio- and stereoselectivity. This reaction is the first example chosen to show the effectiveness of the synthesis supported on onium salts.

The Diels-Alder reaction between a dienophile supported on an onium salt 5 and cyclopentadiene in methylene chloride as solvent was therefore studied according to the following diagram:



In this part of the work the inventors studied in a precise manner the influence of:

1) the length of carbon chain which separates the acryloyl function from the ammonium function

2) the nature of the cation and the anion on the reactivity

3) the recycling of the support

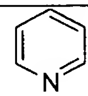
Procedure for the Diels-Alder reaction:

The supported acrylate 5 and 10 equivalents of cyclopentadiene are dissolved in 2 ml of methylene chloride. The solution is then stirred for two hours at ambient temperature. The solvent and the excess of reagent are then eliminated under vacuum then the reaction product is dissolved in methanol in the presence of a few drops of 12 N hydrochloric acid. After twelve hours at reflux, the transesterification is complete and the product **21** is then extracted with pentane.

The results obtained are shown in Table **1**:

Table 1: Influence of the length of the arm (n) and the nature of the onium cation on the reactivity of acrylic ester

test	Y	n	conv (%)
1	Me_3N	0	85
2	Me_3N	1	78
3	Me_3N	4	41

4		1	62
5	$P(Bu)_3$	1	48

The results in the table show that the length of the alkyl chain of the graft arm influences the reactivity of the acrylic ester. Increasing the length of the alkyl chain separating the two ammonium and ester functions reduces the reaction rate. This suggests that an activation of acryloyl due to the electrophilic effect of the trimethylammonium function reduces the electrons of the acrylic double bond and makes it more reactive (compare with tests 1, 2 and 3). Similarly, the nature of the cation influences the reactivity (compare with tests 2, 4 and 5). It must also be noted that the endo/exo selectivity is the same whatever the nature and the composition of the support.

Finally, the possibility of recycling the support was tested in the case of the ammonium salts. The results obtained are shown in Table 2.

Table 2: Recycling of the support 5

test	Yield of ester 21 (2 stages)
1st reaction	78
1st recycling	75
2nd recycling	77
3rd recycling	81

During the recycling operations, a stability in the reactivity, the selectivity and the yield of the reactions was found.

2) Reaction of 5a with various other dienes:

Acrylic acid 5a was used as dienophile in the Diels-Alder reaction with different dienes. For this, a solution of 0.85 mol/l of 5a in acetonitrile is heated at 120°C in sealed tubes in the presence of 0.01% hydroquinone according to the diagram above. After reaction, the reaction mixture is evaporated to dryness then washed with ether. This allowed the isolation of the cycloadducts **22aa-ad** with good yields (Table 3).

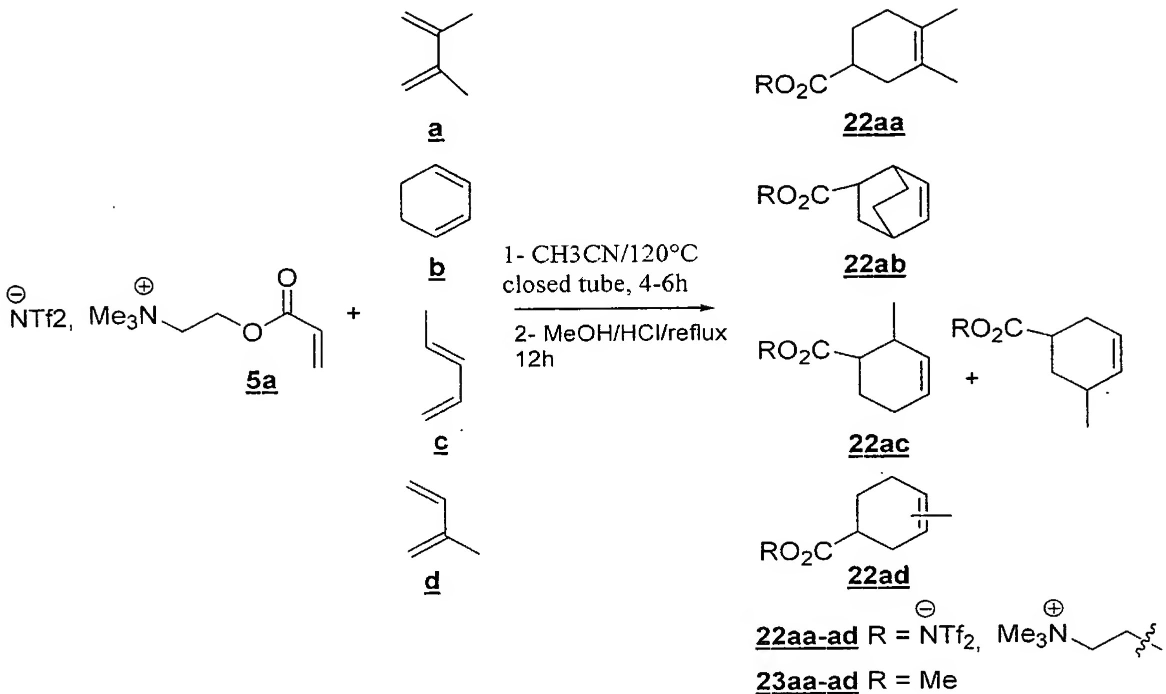
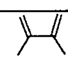
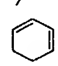
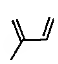
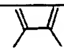
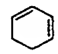
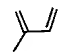


Table 3: Yield of cycloadducts 22aa-ad.

Test	Dienes	Time (h)	Yield (%)
1		4	90
2		6	85
3		4	80
4		4	88

Methyl esters **23aa-ad** are obtained by a transesterification reaction of the cycloadducts **22aa-ad** after 12 hours at reflux of methanol in the presence of a catalytic quantity of hydrochloric acid. Table 4 shows the yields of isolated **23aa-ad**.

Table 4: Yield of cycloadducts 23aa-ad.

23a	Dienes	Yield (%)
23aa		85
23ab		83
23ac		73
23ad		79

B - Example 2: Coupling reactions

The formation of carbon-carbon bonds is a fundamental operation in organic chemistry. Among the many possible reactions, the catalytic methods using organometallic catalysts are extremely important. For our part, we have tested these novel supports in coupling reactions which were already the subject of numerous works on soluble resins and polymers (Franzen, 2000; Bertineina et al.,1998; Wendeborn et al.,1998).

The different coupling reactions studied are as follows:

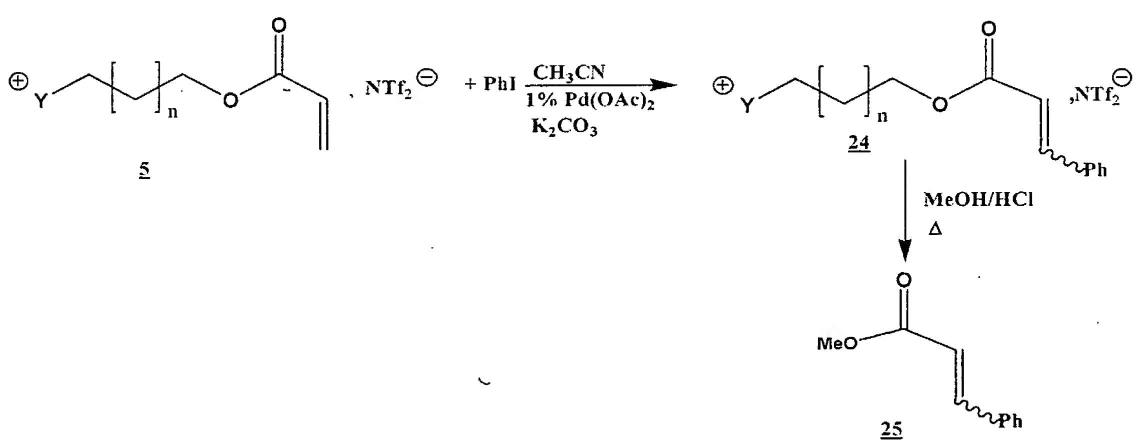
1) Heck coupling
2) Suzuki coupling
3) Sonogashira coupling

In the different examples which follow, we supported acrylic esters, or arylic esters or also the two reagents:

1) Heck Coupling:

→ With a supported acrylic ester

In this example a supported acrylic ester is used in the Heck reaction in the presence of palladium acetate as catalyst, potassium bicarbonate as base and an aryl iodide in a large excess as reagent according to the following diagram:

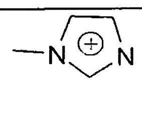
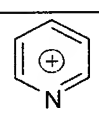


All the coupling reactions were carried out at 100°C. The reactions were monitored with proton NMR (**Figure 1**) (test 3 of Table 5).

Figure 1 illustrates the possibility of the monitoring of the reactions with ^{1}H NMR and its simplicity. The complete disappearance of the signals between 5.9 and 6.5 ppm corresponding to the three protons of the double bond of the substrate **5d**, and the appearance of the signals of the double bond of the coupling product **24** are seen clearly.

The different parameters which influence this reaction were then studied to create the optimal conditions. The results obtained are shown in Table 5:

Table 5: Influence of the nature of the cation, the support and the spacer arm on the Heck coupling reaction

test	A	n	Time (h)	Concentration (mol/l)	Conversion (%)[i]	Yield of 25 isolated	E/Z[ii] ratio
1	$(Me)_3N^{\oplus}$	1	2	0.05	70	-	88/12
2	$(Me)_3N^{\oplus}$	0	1	0.1	100	83	> 99/1
3	$(Me)_3N^{\oplus}$	1	1	0.1	100	86	> 99/1
4	$(Me)_3N^{\oplus}$	4	1	0.1	100	80	> 99/1
5		1	1	0.1	100	85	> 99/1
6		1	1	0.1	87	84	> 99/1
7	$(Bu)_3P^{\oplus}$	1	1	0.1	100	79	> 99/1

i: % of conversion from 5 to 24 determined by NMR.
ii: determined by NMR and confirmed by GC after transesterification.

Tests 1 and 2 show that the concentration of the reaction medium, besides reducing the quantity of the solvent, influences both the reactivity and the selectivity of the reaction. Thus by doubling the concentration, only the trans isomer is obtained.

A direct relationship between the reactivity and the nature of the cation of the supported substrate was noted. In the presence of the pyridinium cation, the reaction

rate is reduced and only 87% of coupling product is formed under the standard conditions. However the length of the alkyl chain separating the acrylic ester and the ammonium function has no influence either on the reactivity, or on the selectivity (compare with tests 2, 3 and 4).

→ With supported iodoaryl ester 6g

The iodoaryl ester supported on ammonium salt 6g was used in the Heck reaction.

A solution (0.85 mol/l) of the salt 6g in DMF is heated to 100 °C, in the presence of palladium acetate as catalyst, potassium bicarbonate as base and a large excess of olefin. The yields of isolated products are shown in Table 6:

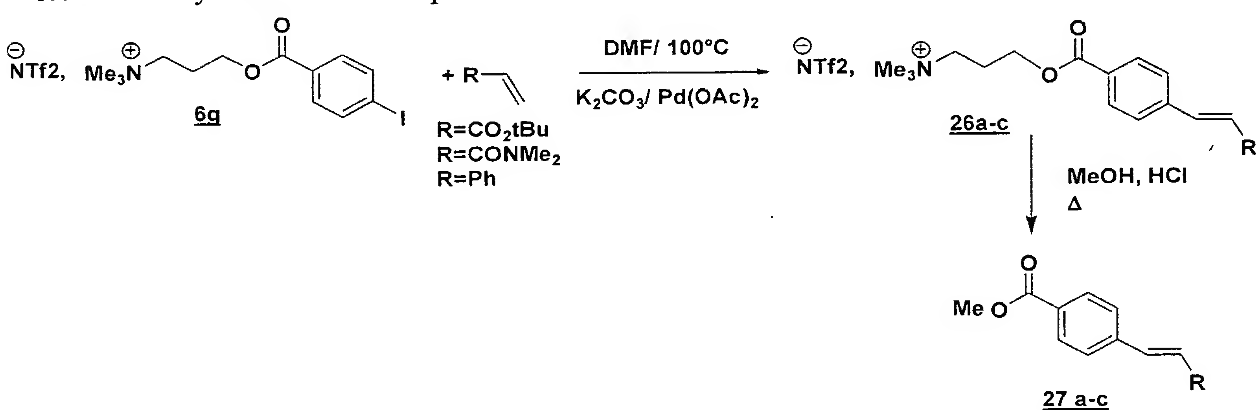


Table 6: Yields of the coupling products 26

N°	R	Quantity of $Pd(OAc)_2$(%)	Yield(%)(Time h)
26a	CO_2tBu	1	84(1)
26b	$CONMe_2$	5	80(3)
26c	Ph	5	80(3)

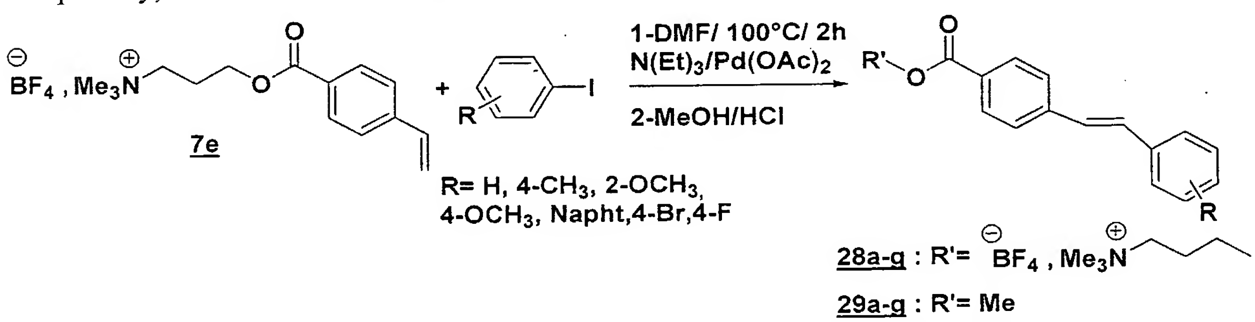
The cleavage of the coupling products is carried out by a transesterification reaction of a mixture of these three salts in the presence of methanol and a catalytic quantity of hydrochloric acid. The reaction is quantitative and the methyl esters obtained are extracted with ether after neutralization with a K_2CO_3 solution and then injected into the GC/MS. The following chromatogram shows the retention times of the different esters (Figure 2 and Table 7).

Table 7: Characterization by GC/MS of the ester library 27

No.	R	Retention time in minutes	Molecular mass
27a	CO_2tBu	14.87	220
27b	$CONMe_2$	20.92	233
27c	Ph	21.24	238

→ With supported styrene 7e

In this example, the styrene 7e is reacted with an equimolecular mixture of 7 different aryl iodides thus leading, after reaction, to a small library of the 7 products 28 or 29. A solution of 0.85 mol/l of 7e in DMF, to which 3 equivalents of triethylamine, 5% palladium acetate and a mixture of the seven aryl iodides in a stoichiometric quantity, is thus introduced into the same well (diagram below).



The progress of the reaction is monitored by HPLC by following the disappearance of the aryl iodides. The mixture of the salts 28a-g is then transesterified by addition of methanol and a catalytic quantity of hydrochloric acid. After evaporation of the solvent, the esters formed 29a-g are extracted with ether and injected into the GC/MS. (Figure 3)

Table 8 shows the allocation of the esters 29 obtained.

Table 8: Characterization by GC/MS of the ester library.

29	R	Retention time	Molecular mass
29a	F	15.46	256
29b	H	15.59	238
29c	CH_3	16.89 and 17.15	252
29d and 29e	2 and 4-MeO	17.33 20.15	268
29f	Br	20.80	317
29g	Naphth	25.36 and 26.00	290

2) Suzuki Coupling:

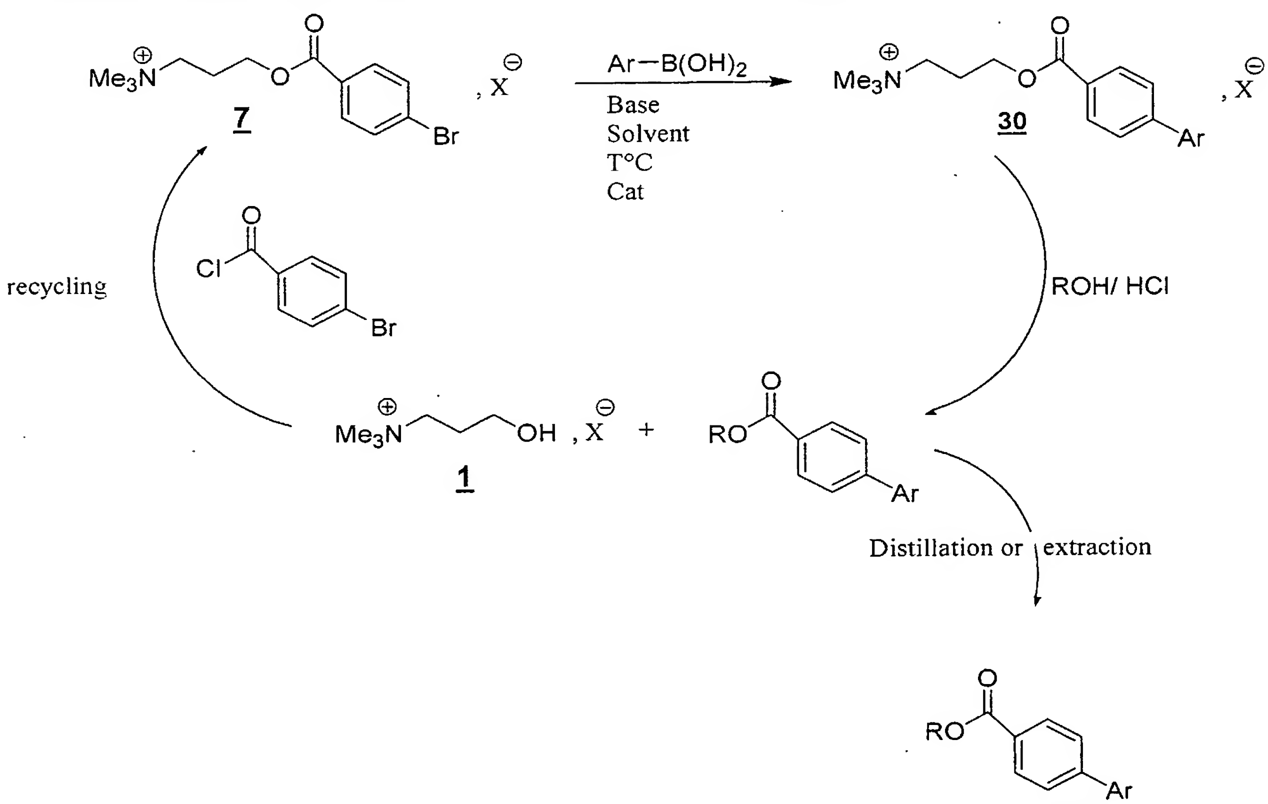
The second example of a coupling reaction where the onium supports were used is the Suzuki reaction which consists of a coupling of an aryl halide with a boronic aryl acid. This study was carried out according to two different approaches:

1) supporting an aryl halide
2) simultaneously supporting an aryl halide and a boronic acid.

∗ Supported aryl halide.

In this study 3-iodobenzoic acid and 4-bromobenzoic acid supported on an onium salt were used, and DMF and dioxane were chosen to be used as solvents often used in this type of reaction on soluble resin or polymer. We therefore studied the effect of the temperature and the anion of the support.

These different studies were carried out using phenylboronic acid and palladium acetate as catalyst according to the following reaction diagram:



31, 32 et 33

with Ar=aromatic ring and R=Me, Et or Pr or Ar'-Ar

Table 9: Influence of the temperature and the solvent on the Suzuki coupling reaction in the presence of K_2CO_3 (2 equivalents) and $Pd(OAc)_2$ (1 molar %).

test	Solvent	X	Temperature (°C)	Conversion rate	Ar-Ar'	Ar-Ar
1	DMF	NTf_2	20 (18h)	99.1	98.7	0.4
2	DMF	NTf_2	80 (5h)	100	96.4	3.2
3	Dioxane	NTf_2	80 (5h)	70	40	30

Examination of Table 9 shows that in DMF after five hours at 80°C, the reaction is complete with an excellent selectivity. By contrast, in the case of dioxane, under the same conditions, 70% conversion was observed with 30% formation of homocoupling product (Ar-Ar). It is to be noted that the desired product is isolated after transesterification with a yield of 95% and 99.9% purity (test 2).

In light of the results obtained during this non-exhaustive study, it was chosen to work under the following conditions for the preparation of a biaryl ester library:

Solvent: DMF

Temperature: 80°C

Base: solid K_2CO_3 for simplicity of the reaction treatment

Precatalyst: $Pd(OAc)_2$

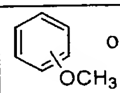
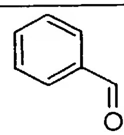
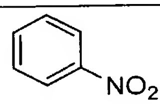
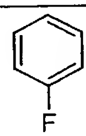
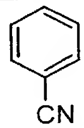
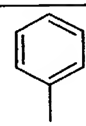
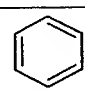
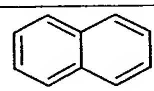
For the preparation of this biaryl ester library, firstly a series of coupling reactions was carried out in parallel with 9 arylboronic acids and supported 4-bromobenzoic acid. Then, the 9 supported biaryl esters are mixed to form a homogeneous solution, which is then divided into three equal portions. After which, each of the solutions is dissolved in a different alcohol after evaporation of the DMF under vacuum. A few drops of concentrated hydrochloric acid (12 N) are then added then the mixture is taken to reflux for 18 hours. After evaporation to dryness, the biaryl ester mixture is extracted with ether. 3 series of 9 esters are therefore obtained and are analyzed by GC/MS. The different biarylesters expected are all obtained quantitatively (no trace of aryl esters corresponding to the starting product was detected by GC/MS) and identified with no ambiguity.

All the results are shown below in Tables 9 to 11 and the chromatograms corresponding to the biaryl ester mixtures represented in Figures 4 to 6.

a/ Biaryl methyl esters 31a-i:

Table **10** below corresponds to the chromatogram of Figure 4.

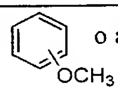
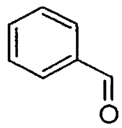
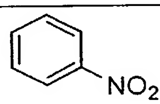
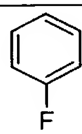
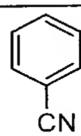
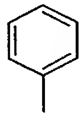
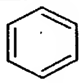
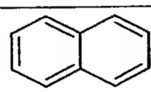
Table 10: GC/MS characteristics of the methyl ester library 31a-i

31	Ar	Retention time	Molecular mass
31a and 31b	 o and p	21.31; 22.35	242
31c		23.24	240
31d		28.58	257
31e		16.28	230
31f		24.23	237
31g		18.25	226
31h		16.41	212
31i		27.74	262

b/ Biaryl ethyl esters 32a-i:

Table **11** below corresponds to the chromatogram of Figure 5.

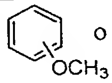
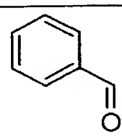
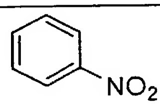
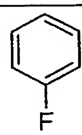
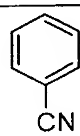
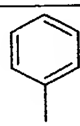
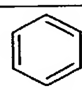
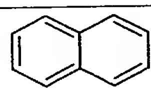
Table 11: GC/MS characteristics of the ethyl ester library 32a-i

32	**Ar**	**Retention time (mn)**	**Molecular mass**
32a and 32b	 o and p	23.76; 24.73	256
32c		25.19	254
32d		28.72	271
32e		17.33	244
32f		25.95	251
32g		19.82	240
32h		17.50	226
32i		30.12	276

c/ Biaryl propyl ester 33a-i

Table 12 below corresponds to the chromatogram of Figure 6.

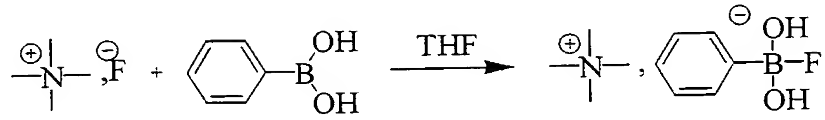
Table 12: GC/MS characteristics of the propyl ester library 33a-i

33	Ar	Retention time in minutes	Molecular mass Determined by MS
33a and 33b	 o and p	26.42, 27.36	270
33c		28.13	268
33d		32.29	285
33e		19.28	258
33f		28.96	265
33g		22.82	254
33h		19.53	240
33i		34.52	290

* **Simultaneously supported aryl halide and boronic acid:**

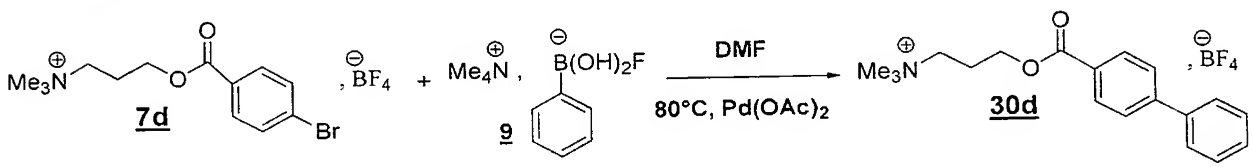
An arylboronic acid was grafted to an anion in order to then engage it in a releasing Suzuki coupling reaction.

Phenylboronic acid is grafted onto an onium support via the anion. If the anion X^- of the support salt is fairly nucleophilic, it will react with the phenylboronic acid quaternizing the boron atom in order to produce a borate. The nucleophile of choice is fluoride.



This quaternarization reaction was carried out by dissolving, at ambient temperature, tetramethylammonium fluoride in THF (anhydrous) then addition of phenylboronic acid. After stirring at ambient temperature for 18 hours, the precipitate which forms is filtered then washed with ether. The yield of isolated product is of the order of 80%. The monitoring of this reaction took place using boron and fluorine NMR.

The Suzuki coupling is carried out under the same conditions as those described in the first part, between supported 4-bromobenzoic acid and supported phenylboronic acid according to the following reaction diagram:



The reaction leads to the coupling product with an excellent yield (98% of pure isolated product after transesterification) and a reactivity greater than that observed in the case of phenylboronic acid. The support **1d** is recovered quantitatively and can be reused.

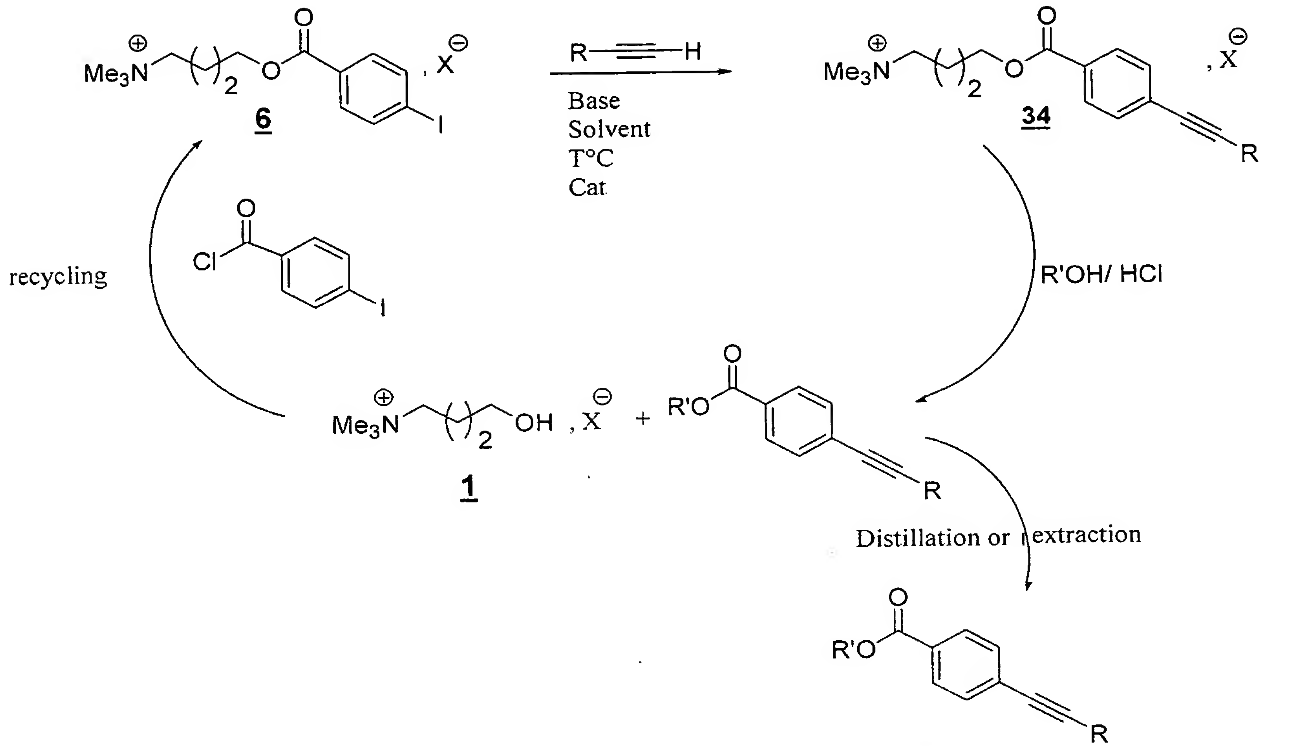
3) Sonogashira coupling:

Another example of coupling where this family of soluble supports was tested is that of Sonogashira which consists in a coupling of an aryl halide and a true alkyne. This study was carried out by supporting aryl halide or alkyne on an onium salt.

- **Supported aryl halide:**

Firstly and in order to create the optimal conditions, the influence of the different parameters on the coupling reaction was studied. Therefore the effect of the temperature, of the nature of the solvent, of the catalyst, of the base and of the counter-ion of the ionic support were examined.

These different studies were carried out using 4-iodobenzoic acid according to the following reaction diagram:

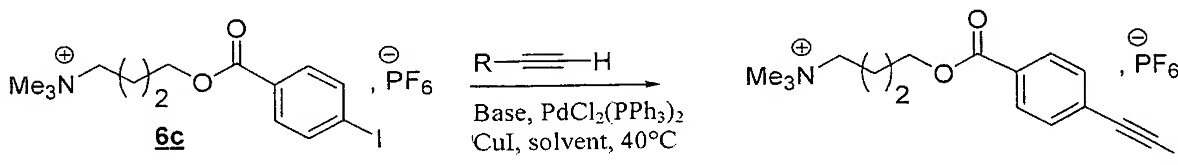


35(R'=Me), 36(R'=Et), 37(R'=Pr) et 38(R'=Bu)

(R = Me, And, Pr or Bu)

1 - Effect of the nature of the solvent and the base:

This study was carried out using 2.5 % catalyst, 5 % CuI and a temperature of 40°C in order to determine the influence of the nature of the base and the solvent on the coupling reaction. The nature of the base or the solvent was therefore varied:



The different tests carried out at 40°C after 1 hour of reaction are shown in Table 13:

Table 13: Sonogashira coupling at 40°C for 1 hour (influence of the base and the solvent)

test	base	Solvent	Conv. rate (%)
1	K_2CO_3(s)	CH_3CN	57[i]
2	$N(Et)_3$	CH_3CN	100[i]
3	$N(Et)_3$	DMF	100[ii]
4	$N(Et)_3$	THF	75[ii]
5	$N(Et)_3$	Toluene	65[ii]
6	$N(Et)_3$	CH_2Cl_2	100[ii]
7	$N(Et)_3$	Acetone	100[ii]
8	$N(Et)_3$	Dioxane	100[ii]
9	$N(Et)_3$	CH_3CN	100[ii]

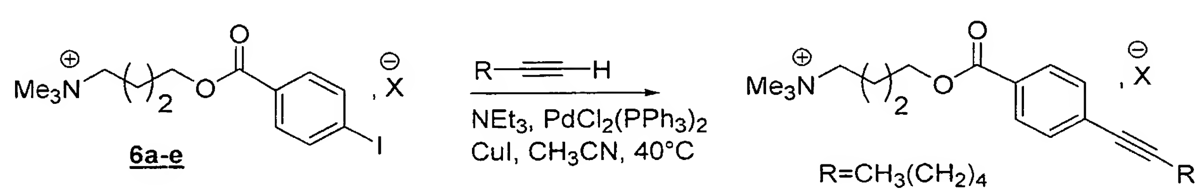
i: X = PF_6; R = butyl
ii: X = NTf_2; R = pentyl

Examination of Table 13 shows that the use of triethylamine allows better reactivity to be observed compared with the use of solid potassium bicarbonate as base (compare tests 1 and 2).

Tests 2 to 8 show that various conventional organic solvents can be used. However, a reduction of reactivity was observed in the cases of toluene and of tetrahydrofuran where the reaction medium is heterogeneous.

2 - Effect of the nature of the anion of the onium salt:

The comparative study was carried out on the coupling reaction of 1-heptyne on N,N',N''-trimethylbutylammonium 4-iodobenzoate, using acetonitrile as solvent, triethylamine as base and $PdCl_2(PPh_3)_2$ as catalyst, according to the following reaction diagram:



The results obtained after 15 minutes of stirring at 40°C are shown in the following Table 14:

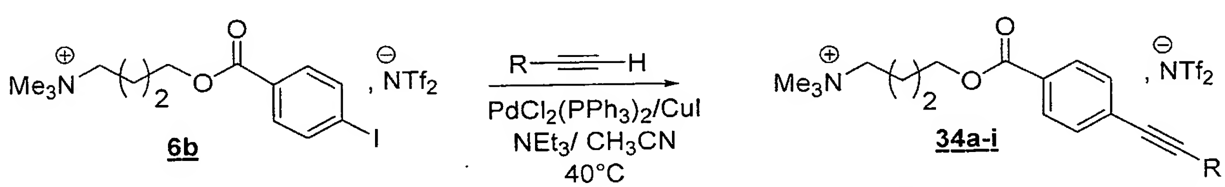
Table 14: Sonogashira coupling (15' at 40°C): influence of the anion.

test	X	Conversion rate (%)
1	I	50
2	NTf_2	100
3	BF_4	70
4	PF_6	97
5	CH_3SO_4	95
6	CF_3SO_3	91

Examination of Table 14 shows that the coupling reaction takes place whatever the nature of the anion. On the other hand, a better reactivity is observed in the case of triflate, methylsulphate, hexafluorophosphate and bis-trifluoromethane sulphonamide (triflimide).

3 - Effect of the nature of alkyne:

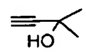
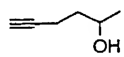
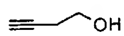
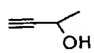
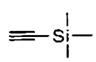
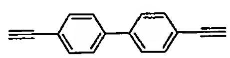
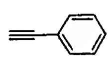
In order to generalize this methodology the coupling of the supported aryl halide 6b with various fonctionnalized or non-functionalized alkynes was carried out.



These different reactions were monitored with proton NMR. Figure 7 shows the simplicity and the ease of interpretation of such spectra.

The results obtained by varying the alkynes are shown in Table 15.

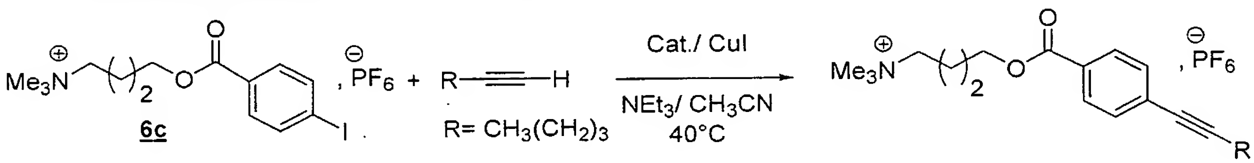
Table 15: Sonogashira coupling of 6b with different alkynes.

test	Alkyne	Reaction time (h)	Conv. rate (%)	Yield[i] (%)
1		1	100	85
2		1	100	75
3		1	100	92
4		1	100	83[ii]
5		1	100	88
6		1	100	77
7		1	100	95
8		1	100	63[ii]
9		1	100	94

i: Yield of pure isolated product.
ii: Yield of product isolated after transesterification with methanol.

4 - Effect of the nature and the quantity of the catalyst:

The coupling reaction of N,N,N-trimethylbutylammonium 4-iodobenzoate and hexyne was carried out in the presence of triethylamine as base and acetonitrile as solvent according to the following reaction diagram:



The results obtained are shown in the following Table 16:

Table 16: conditions for Sonogashira coupling in acetonitrile of iodoaryl 6c with 1-hexyne.

test	catalyst	cata/CuI (% / %)	Temperature (°C)	Reaction time (h)	Conversion rate (%)[i]
1	$PdCl_2(PPh_3)_2$	10/20	20	0.2	100[ii]
2	$PdCl_2(PPh_3)_2$	10/20	40	0.2	100[ii]
3	$PdCl_2(PPh_3)_2$	5/10	20	0.2	100
4	$PdCl_2(PPh_3)_2$	2.5/5	20	0.2	100
5	$PdCl_2(PPh_3)_2$	1/2	20	1	70
6	$PdCl_2(PPh_3)_2$	2.5/0	20	0.2	< 10%
7	$PdCl_2(PPh_3)_2$	2.5/5	40	0.2	100
8	$PdCl_2$	2.5/5	40	0.2	<10
9	$Pd(OAc)_2$	2.5/5	40	0.2	<10

i: yield determined by NMR.
ii: yield determined by GC/MS after transesterification.

The following points are noted:

- the reaction takes place at ambient temperature with record times even in the presence of 2.5% catalyst. These results are very advantageous given that, in the case of the solid support the same reaction is complete only after 24 hours in the presence of 10% catalyst;
- the presence of phosphorated ligand clearly accelerates the reaction, and the $PdCl_2(PPh_3)_2$ remains, by far, the catalyst of choice for this reaction (compare with tests 7, 8 and 9);
- the reactivity remains identical while reducing the percentage of catalyst from 10 to 2.5%. By contrast, reduction to 1% causes a fall in the reactivity (test 5). Similarly, Test 6 shows that the presence of CuI is not essential but it accelerates the reaction.

5 - Application in combinatorial chemistry:

After analyzing the results obtained during this study, it was decided to work under the following conditions for the preparation of an aromatic alkyne library:

Solvent: CH_3CN

Temperature: 40°C

Base: Triethylamine

For the preparation of this ester library the procedure was as follows:

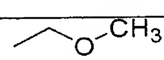
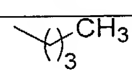
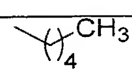
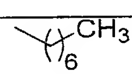
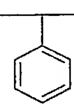
Firstly, a series of coupling reactions in parallel with 5 alkynes and supported 4-iodobenzoic acid was carried out. Then, the 5 reaction media were mixed to form a homogeneous solution. After evaporation of the acetonitrile and washing with ether, the residue is then divided into four equal portions. Each part is dissolved in an alcohol in the presence of 3 drops of concentrated hydrochloric acid (12 N) then the mixture is taken to reflux for 18 hours. After evaporation to dryness of the alcohol, the mixture of the products is extracted with ether. The 4 series of 5 alkynes obtained are then analyzed in GC/MS. The different alkynes expected are all identified with no ambiguity.

The results obtained are listed below in the form of tables. The chromatograms of the mixtures of alkynes are also given (Figures 8 to 11).

a/ Acetylenic methyl esters __35a-e__:

Table 17 below corresponds to the chromatogram of Figure 8.

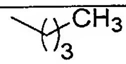
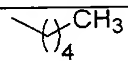
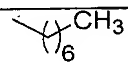
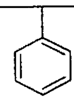
Table 17: Characterization by GC/MS of the methyl ester library

__35__	R	Retention time in minutes	Molecular mass
__35a__		14.57	204
__35b__		15.35	216
__35c__		16.56	230
__35d__		20.53	236
__35e__		21.16	258

b/ Ethyl esters __36a-e__:

Table 18 below corresponds to the chromatogram of Figure 9.

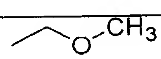
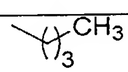
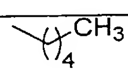
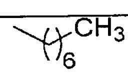
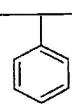
Table 18: Characterisation by GC/MS of the ethylic ester library

<u>36</u>	R	Retention time	Molecular mass
<u>36a</u>		15.24	218
<u>36b</u>		16.18	230
<u>36c</u>		17.68	244
<u>36d</u>		22.77	250
<u>36e</u>		23.57	272

c/ Propyl esters <u>37a-e</u>:

Table 19 below corresponds to the chromatogram of Figure 10.

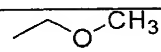
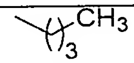
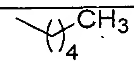
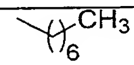
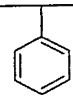
Table 19: Characterization by GC/MS of the propyl ester library

<u>37</u>	R	Retention time	Molecular mass
<u>37a</u>		16.41	232
<u>37b</u>		17.68	244
<u>37c</u>		19.78	258
<u>37d</u>		25.70	264
<u>37e</u>		26.33	286

d/ Butyl ester <u>38a-e</u>:

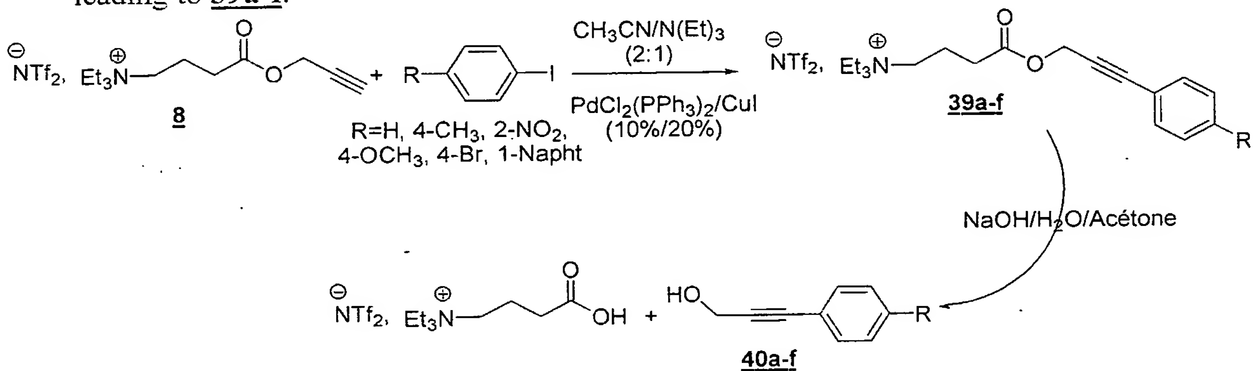
Table 20 below corresponds to the chromatogram of Figure 11.

Table 20: Characterization by GC/MS of the butyl ester library

<u>38</u>	R	Retention time	Molecular mass
<u>38a</u>		16.41	232
<u>38b</u>		17.68	244
<u>38c</u>		19.78	258
<u>38d</u>		25.70	264
<u>38e</u>		26.33	286

- **Supported alkyne <u>8</u>:**

We used the supported alkyne <u>8</u> in the Sonogashira reaction with different iodides. This occurred in the presence of $PdCl_2(PPh_3)_2$ as catalyst and CuI as co-catalyst. After 20 minutes of stirring at ambient temperature, the reaction is complete leading to **<u>39a-f</u>**.



After reaction, the reaction mixtures are evaporated to dryness and washed with ether in order to eliminate the excess of reagents. The oils thus obtained are dissolved in methylene chloride then the solutions are washed with an aqueous solution of K_2CO_3 to release Et_3N from its hydrochloride formed during the reaction. After treatment with Na_2SO_4 and evaporation of the methylene chloride, the salts are isolated with a good yield. This is illustrated in Table 21.

Table 21: Yield of products 39a-f

Input	R	Yield(%)
39a	H	77
39b	4-CH_3	89
39c	2-NO_2	81
39d	4-OCH_3	92
39e	4-Br	80
39f	1-Naphth	86

The alcohols formed are extracted with ether after saponification in the presence of an aqueous solution of 5% NaOH in water of the mixtures of the previously isolated salts and then injected into the GC-MS (Figure 12 and Table 22).

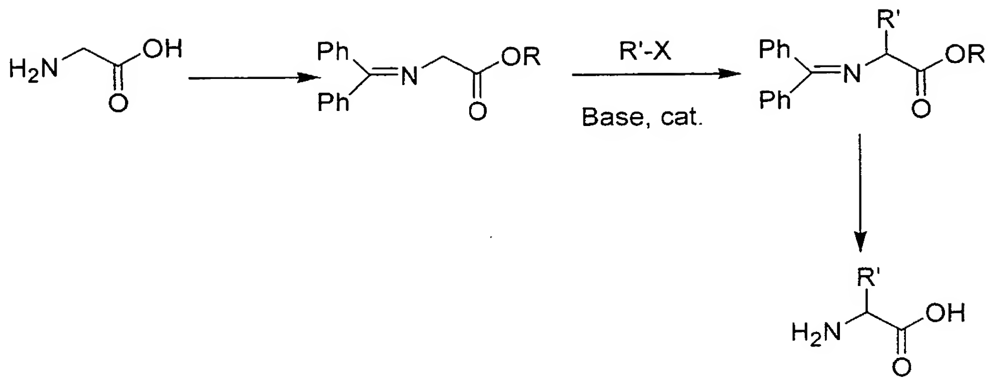
Table 22: Characterization by GC/MS of the alcohol library 40a-f

40	R	Retention time	Molecular mass
40a	H	11.47	132
40b	4-CH_3	12.40	146
40c	2-NO_2	13.07	177
40d	4-OCH_3	13.59	162
40e	4-Br	13.71	211
40f	1-Naphth	16.15	182

C - Example 3: Synthesis of α-amino acids:

The alkylation of the imines derived from glycine and benzophenone was chosen as a model reaction in order to explore the potential of the onium salts as supports in this type of reaction. The advantage of these substrates resides in particular in the possibility of obtaining substituted α-amino acids and optionally carrying out their asymmetric synthesis.

The sequence used uses the alkylation of an iminoester derived from glycine and benzophenone under the phase transfer conditions according to the method described by O'Donnel et al. (1989) in solution and allows synthesis of the higher amino acids according to the following diagram:



Besides the twenty one natural (L)-α-amino acids known and isolated from protein hydrolyzate, other unnatural (L)-α-amino acids have useful biological properties. For example, the incorporation of an amino acid having well chosen substituents into a peptide can produce conformational constraints and increase the selectivity for a receptor. For example the inhibition of the decarboxylases, hydrolases or transferases by an α-alkyl amino acid which plays the role of a suicide substrate can be mentioned (Williams, R.M. "Synthesis of Optically Active α-Amino Acids" Pergamon Press, Oxford, 1989).

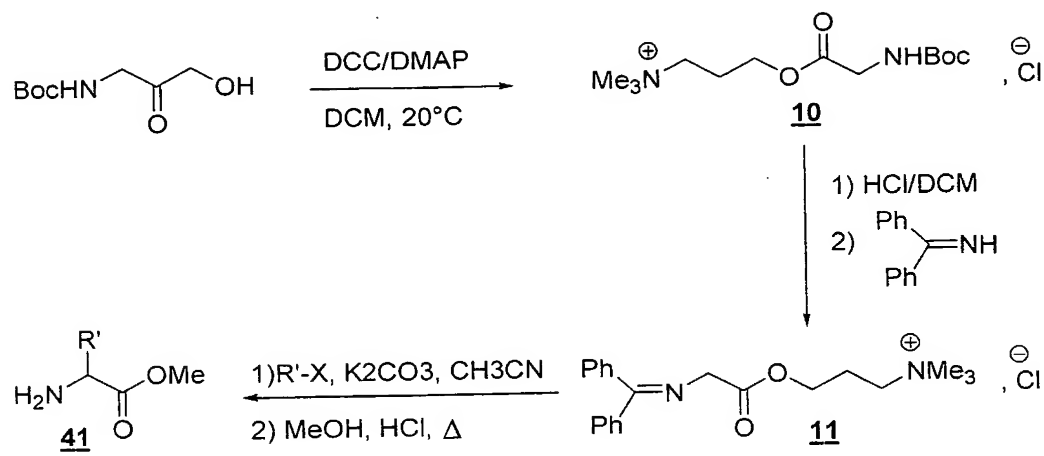
(D)-phenylglycine (A) and (D)-p-hydroxyphenylglycine (B), marketed by the Dutch company DSM, respectively constitute the raw materials for the production of the antibiotics ampicillin (A) and amoxicillin (B). Sales of these reach 1.5-1.7 billion dollars per year.

Despite the increased demand for α-amino acids, fermentation remains the main method for their preparation. Since the end of the 80s, methods of synthesis have seen their use become established in industry. The unnatural α-amino acids are obtained by two methods:

- asymmetric synthesis.
- cleavage which remains the method of choice.

Moreover, the synthesis on a solid or soluble PEG-type support is still one of the most effective and simple methods to use in order to attain these molecules (Lindström et al., 2002).

The onium salts were therefore tested as soluble supports for the preparation of the higher α-amino acids according to the following reaction diagram:



R'=Bu Yield=73%
R'=Allyl Yield=82%

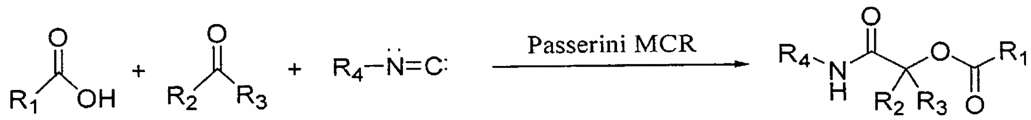
The esterification reaction is carried out directly on N-Boc-glycine in the presence of one equivalent of DCC and 5% DMAP at ambient temperature in dichloromethane (DCM). The Boc protective group is then eliminated in the presence of hydrochloric acid in DCM with a good yield. Similarly, the condensation of amino ester with diphenylmethylene imine leads to the imino ester **11** with an excellent yield and which can be preserved for several days at ambient temperature.

It is to be noted that the support which is an ammonium salt also plays the role of phase transfer catalyst in the stage of alkylation of the Schiff's base **11**, and we have found a greater reactivity than that described in the literature for the alkylation of the same substrate supported on PEG or a solid support.

D - Example 4: Multi-component reactions MCR

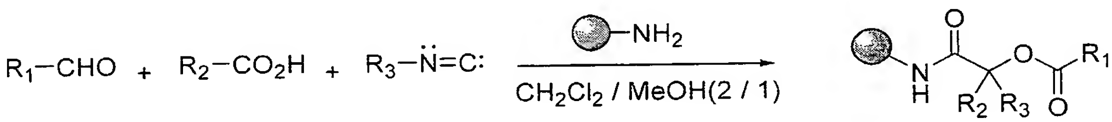
Multi-component reactions simultaneously bring together at least three partners under experimental conditions which do not vary over time and allow the creation of several covalent bonds in cascade in a single reactor, by contrast to standard reactions where two reagents lead to a product by creation of a new bond. Thus it is possible to attain a highly functionalized molecule from relatively simple entities in a single stage. Moreover the MCRs combine convergence and economy of atoms, two essential principles in organic synthesis and also in combinatorial chemistry. Finally it is pointed out that these reactions generally take place with a high yield, because they avoid the succession of stages of linear or multi-stage syntheses which, at each stage, cause a drop in yield.

The best known and most highly developed MCRs are those of Passerini and of Ugi. One of the main reagents of these reactions is an isonitrile of general formula RN=C, in which the electron structure of the terminal carbon includes a doublet and an electron hole (carbenic type structure) and allows the transition from a carbon atom which is strictly divalent to a tetravalent carbon atom by adding an electrophile **and** a nucleophile. The following diagram represents an example of a Passerini reaction (3CC reaction for 3-component condensation).



α-acyloxyamide

The MCRs were of course transposed onto a solid support. For example a resin with an amine termination was used in a Ugi type reaction in order to lead, after cleavage, to a series of adducts with high purity with yields ranging from average to excellent:



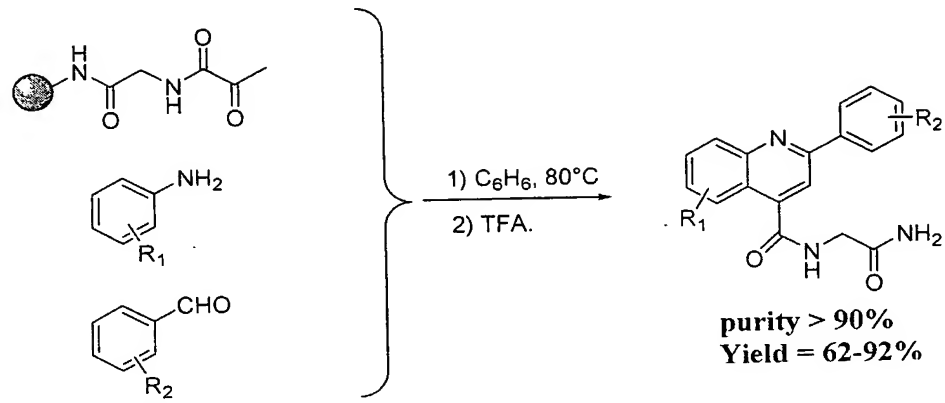
$R_1 = C_6H_{11}, C_6H_5$, *i*Pr
$R_2 = C_6H_{11}, C_6H_5$, Et
$R_3 = C_6H_{11}$

purity > 95%
Yield = 40-95%

Although the Ugi and Passerini reactions are the best known and most highly developed, other MCRs exist, which satisfy the essential criteria that all the reagents are present from the start of the reaction and the conditions do not vary during these reactions. By contrast to the Ugi and Passerini reactions, these other reactions do not rely on the use of an isonitrile as one of the main players in the creation of new covalent bonds. These different types of reactions allow highly functionalized structures which are varied in a single stage to be attained.

- **Synthesis of substituted quinolines according to the Grieco reaction:**

Substituted quinolines are useful pharmacophores. Their synthesis on a solid support was carried out with a so-called Doebner MCR, using an aniline, an aldehyde and an α-dicarbonyl compound. The quinolines are obtained with high purity and very good yields.

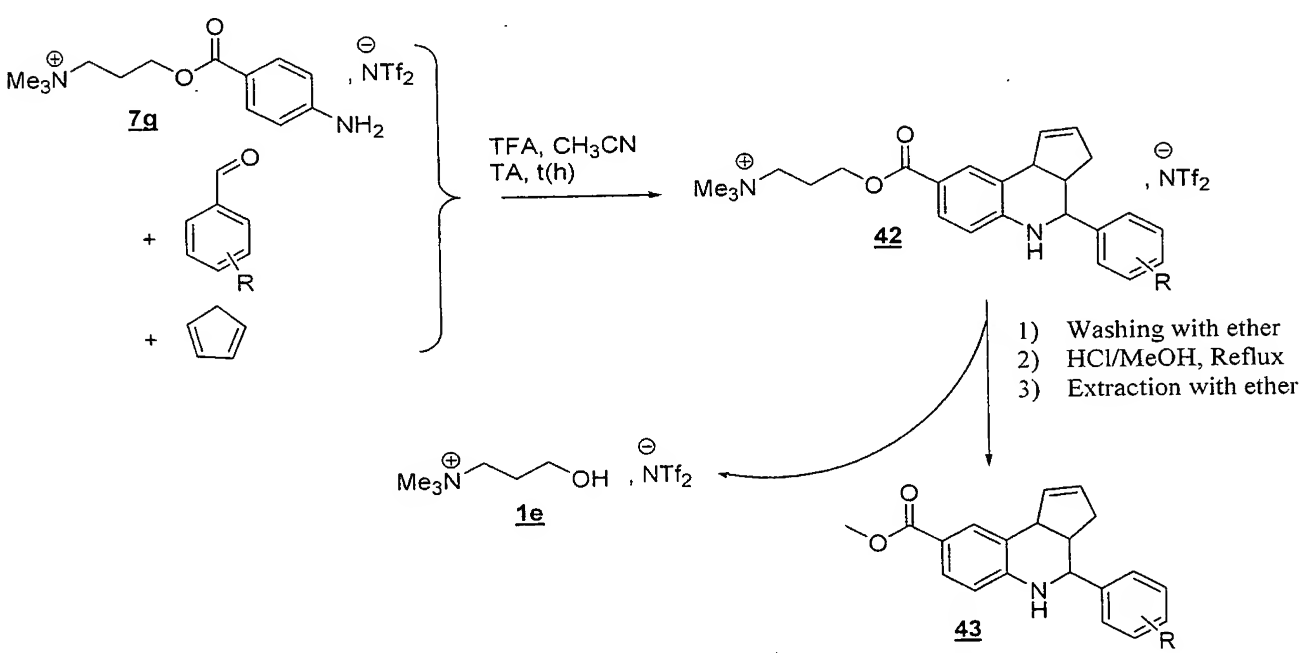


R_1 = H, OCH_3
R2 = H, 4-NO_2, 4-CN, 4-Cl

It was decided here to profit from the numerous advantages offered by the onium supports, as demonstrated in the various examples described previously. Thus, it was decided to test them in Grieco-type MCRs (Grieco et al., 1988). This example has been the subject of several works described by W. Armstrong et al. (1997 and 1998) on a solid support and it allowed the preparation of a library of 80 products with yields ranging from 50 to 93%.

a- Use of supported aniline <u>7g</u> in the Grieco reaction:

In order to do this, the aniline <u>7g</u> was supported, and brought into the presence of an aldehyde and cyclopentadiene in order to produce tetrahydroquinolines. This three-component example consists of a first condensation of aldehyde and aniline in order to produce imine. This then reacts in what is strictly a Diels-Alder reaction with cyclopentadiene in the presence of a catalytic quantity of trifluoroacetic acid.



R= 4-NO_2, H, 4-Cl, 2-MeO

The monitoring of the different reactions was carried out by ^{1}H NMR **(Figure 13)** and a conversion ranging from 80% to 100% was observed according to the nature of the aldehyde. In the presence of electron-rich aldehyde the reaction is slowed down. Thus in the presence of 4-nitrobenzaldehyde the reaction is complete after 12 hours while progress is only 70% in the case of benzaldehyde. The above reaction diagram illustrates the case of 4-nitrobenzaldehyde, after evaporation of the solvent (CH_3CN) and washing with ether in order to eliminate the excess of the two reagents and the trifluoroacetic acid. This diagram also shows that the monitoring of a reaction which leads to complex compounds is possible and with a remarkable clarity. Transesterification with methanol leads to very clean products which are extracted with ether and purified by filtration on silica.

The various examples that we have produced and the results obtained are shown in Table 23 below.

Table 23: Grieco reaction carried out on ammonium salts used as soluble support:

R	Time in (h)	Yield of 42 in (%)	Yield of 43 in (%)
4-NO_2	12	98	82
H	12	70	68
4-OMe	12	60	54
4-Cl	14	96	83

Example: synthesis of tetrahydroquinoline 43 derived from benzaldehyde:

100 mg of supported amine 7g, 500 μl of a 1 M solution of para-nitrobenzaldehyde in acetonitrile, 500 μl of a 1 M solution of cyclopentadiene in acetonitrile and 50 μl of a 1% TFA solution in acetonitrile are mixed under a flow of argon. The reaction mixture is stirred overnight at ambient temperature. After evaporation to dryness and washing with ether, a yellow solid is obtained.

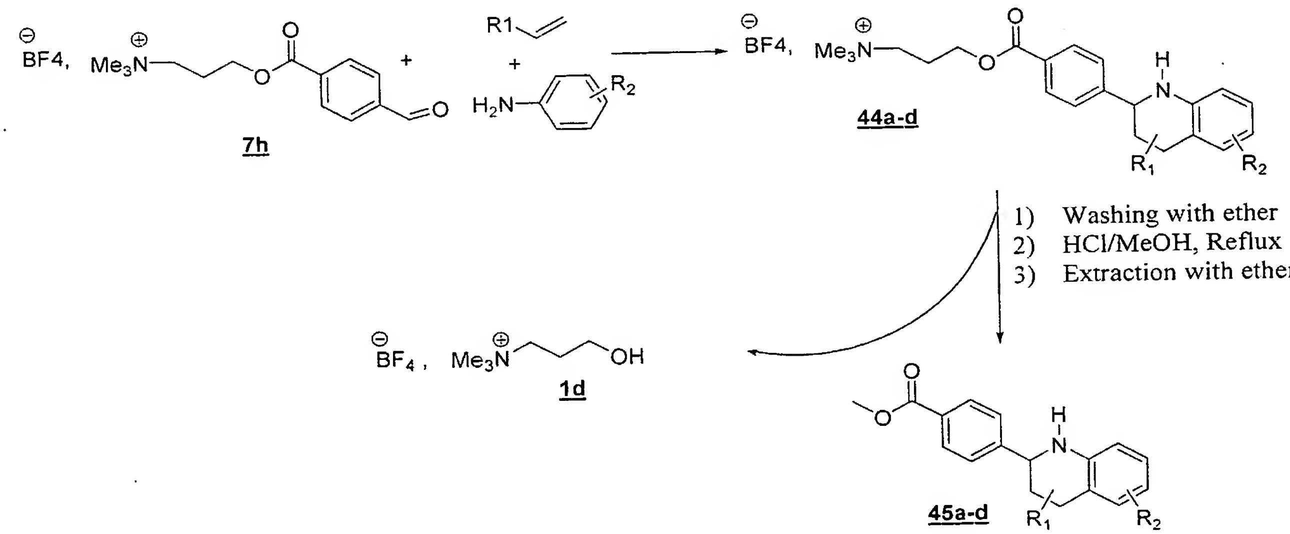
Yield = 71%

^{1}H NMR (200 MHz, Acetone D_6): 1.55-1.8 (m, 1H); 2.35-2.58 (m, 3H); 3.01-3.2 (m, 1H); 3.4 (s, 9H); 3.7-3.9 (m, 2H); 4.1-4.22 (m, 1H); 4.42 (t, 2H, J = 5.81 Hz); 4.9-5.0 (m, 1H); 5.58-5.75 (m, 1H); 5.7-5.8 (m, 1H); 5.93-6.05 (m, 1H); 6.9 (d, 1H, J = 8.4 Hz); 7.6- 7.95 (m, 4H); 8.28 (d, 2H, J = 8.6 Hz).

^{13}C NMR (50 MHz, Acetone D_6): 22.92; 31.25; 45.35; 45.40; 52.96 (t, J_{C-N} = 4.07 Hz); 56.46; 60.67; 64.28; 115.40; 119.45; 120.13 (q, J_{C-F} = 321.194 Hz), 123.40; 124.65; 127.68; 128.17; 129.70; 130.98, 134.26; 147.20; 150.12; 150.50; 165.77

b- Use of the supported aldehyde 7h in the Grieco reaction:

In this work, the supported aldehyde 7h was used in the Grieco reaction with different amines and olefins, in acetonitrile as solvent and in the presence of TFA as catalyst as shown in the following diagram:



After stirring a solution of 0.85 mol/l of 7h in acetonitrile in the presence of 1.2 equivalents of TFA, 1 equivalent of amine and 2 equivalents of olefin at ambient temperature for two hours, the monitoring of the reaction carried out by HPLC shows that it is complete after 2 hours. After the addition of ether the salts formed 44a-d are isolated by filtration followed by a stage of washing with ether. The products 45a-d are isolated by extraction with ether after a transesterification reaction at reflux of the methanol in the presence of a catalytic quantity of hydrochloric acid. The medium is then neutralized by adding a diluted solution of K_2CO_3 after evaporation of the solvent. Table 24 shows the yields of 44 and 45 isolated.

Table 24: Yields of products 44 and 45 isolated.

Products	R_1	R_2	Yield of 44 in %	Yield of 45 in %
44a	Cyclopentadiene	3-NO_2	90	85
44b	Cyclopentadiene	4-Br	88	77
44c	Cyclopentadiene	H	77	70
44d	Indene	4-Br	92	67

Example: Synthesis of 44c:

1 eq of aniline, 2 eq of cyclopentadiene and 1.2 eq of TFA are added to a solution of 100 mg (0.3 mmol) of **7h** in 0.4 ml of acetonitrile. The reaction mixture is stirred for two hours at ambient temperature, evaporated to dryness and then washed with ether. The product of the reaction is isolated by filtration after crystallization in ether.

^1H NMR (300 MHz, Acetone D_6): 1.58-1.75 (m, 1H); 2.40-2.65 (m, 3H); 2.97-2.98 (m, 1H); 3.00-3.15(m, 1H); 3.40 (s, 9H); 3.77-3.92 (m, 2H); 4.03-4.15 (m, 1H); 4.46 (t, 2H, J = 5.94 Hz); 4.68-4.76 (m, 1H); 5.55-5.62 (m, 1H); 6.58-7.13 (m, 4H); 7.60 (d, 2H, J = 8.3 Hz); 8.05 (d, 2H, J = 8.4 Hz).

^{13}C NMR (75 MHz, Acetone D_6): 23.58; 32.19; 46.69; 47.06; 53.67 (t, J = 3.8 Hz); 58.16; 62.42; 64.81; 117.00; 119.49; 126.47; 126.88; 127.59; 129.52; 129.63; 130.18; 130.43; 135.44; 146.90; 149.82; 166.57.

Mass spectrometry (APCI) for $[C_{25}H_{31}N_2O_2][BF_4]$:	
Theoretical mass calculated for (C^+)	391.5
Mass found	391.4

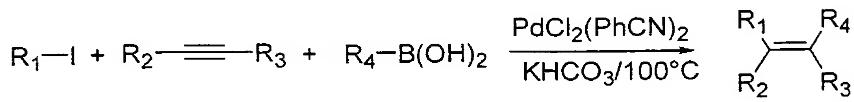
- **Synthesis of tetrasubstituted olefins:**

a- Individual synthesis of tetrasubstituted olefins:

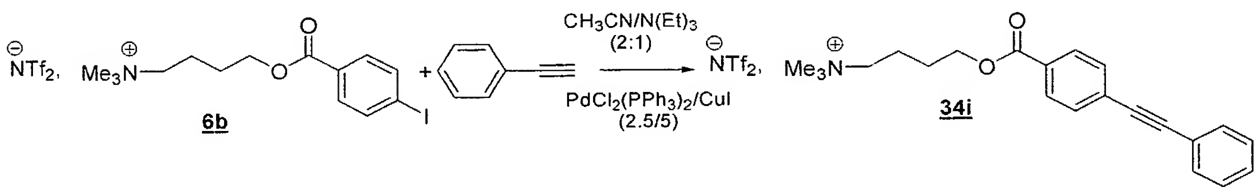
Tetrasubstituted olefins can be obtained by a McMurry reaction or by a Wittig olefination reaction. However, the regio- and stereoselectivities are the main problems associated with these two methods. Other approaches use the carbolithiation of alkynes, reactions of oxiranes carrying a CF_3 group, organosilanes, electrotelluration. However, these approaches generally use reagents which are not readily available and are also sometimes accompanied by insufficient regio- and stereoselectivity.

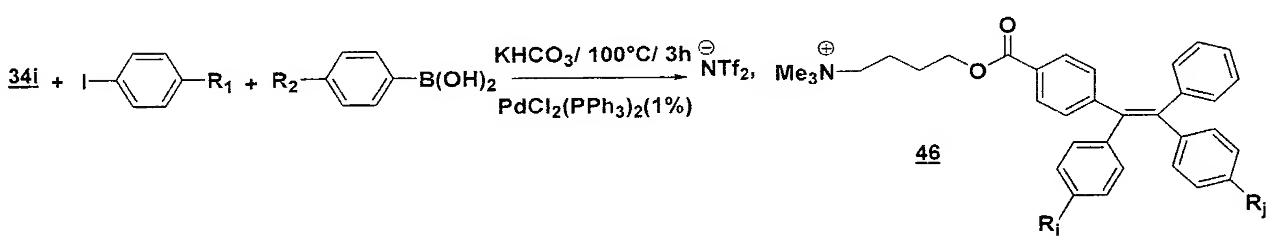
Tetrasubstituted olefins can be prepared by an intermolecular addition reaction of an arylpalladium intermediate with an internal alkyne, followed by a coupling reaction with the organometallic derivatives of boron, tin or zinc.

In 2003, Zhou et al. developed a method for the synthesis of tetrasubstituted olefins using palladium as catalyst. This method uses the intermolecular coupling of an iodoaryl, an internal alkyne and an arylboronic acid[7].



These olefins were synthesized on an onium salt support. In order to do this, as internal alkyne the salt 34i, obtained by Sonogashira reaction between the supported iodide 6b and phenylacetylene, is used. The reaction is carried out at 100°C in a DMF/H_2O mixture (80/20) as solvent, $KHCO_3$ as base and $PdCl_2$ $(PPh_3)_2$ as catalyst.





i = 1 or 2
j = 2 or 1 respectively

Table 25 shows the yields of isolated salts 46 after heating at 100°C for 3 hours.

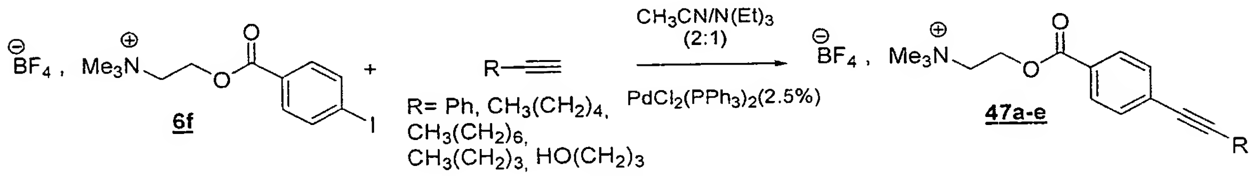
Table 25: Synthesis of olefins* 46.

Input	R_1	R_2	Yield(%)
1	H	H	67
2	CH_3	H	60
3	CH_3O	H	70
4	H	1-Naphth	68
5	CH_3O	1-Naphth	86
6	CH_3	1-Naphth	83

* Mixture of 2 regioisomeric olefins

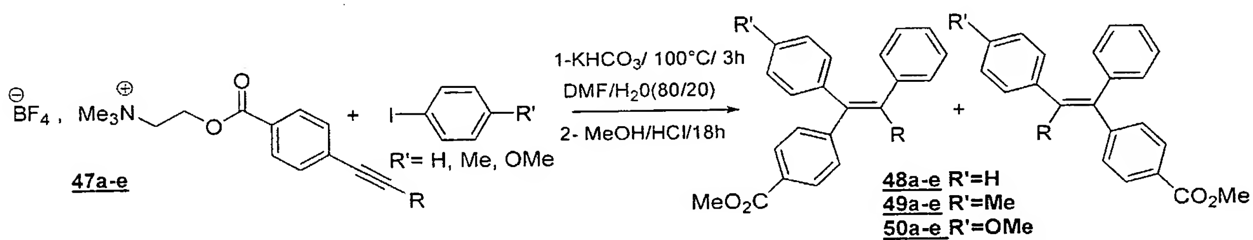
b- Synthesis of tetrasubstituted olefins 47 in a mixture:

The supported iodide 6f is used in the same well and under the same conditions as previously in the Sonogashira reaction in the absence of CuI with five different alkynes.



The monitoring of the reaction by HPLC shows the appearance of the Sonogashira coupling products 47 for which the retention times are 1.92, 3.09, 5.33, 6.57 and 9.35 after overnight stirring at ambient temperature (Figure 14).

After evaporation to dryness of the solvent and washing with ether, the mixture obtained is divided into three parts. Each part is used to form tetrasubstituted olefins without the addition of catalyst. This occurs in the presence of phenylboronic acid and three aryl iodides. After heating at 100°C for three hours the reaction mixtures are transesterified separately in the presence of methanol and hydrochloric acid.



Tetrasubstituted olefins are extracted with ether after evaporation of methanol and injected into the GC/MS. The chromatogram presented in Figure 15 illustrates the case of 4-iodotoluene (**49a-e**).

Table 26: Characterization by GC/MS of the tetrasubstituted olefin library 49a-e.

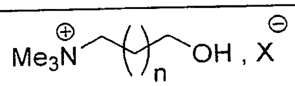
49	R	Retention time	Molecular mass
49a	$CH_3(CH_2)_3$	31.37 and 31.59	384
49b	$CH_3(CH_2)_4$	33.12 and 33.42	398
49c et49d	$HO(CH_2)_3$ and Ph	37.50-38.50	386 and 404
49e	$CH_3(CH_2)_6$	38.80	426

E - INCREASE IN THE PRODUCTIVITY OF THE ONIUM SALT SOLUTIONS IN CONVENTIONAL POLAR SOLVENTS.

It is pointed out that the specific charge of a support is defined by the quantity of reagent which can be supported per gram of support and is expressed in mmol/g. This corresponds to what could be called a ***specific functionality*** of a support denoted ***f*** which could be expressed in millifunctions per gram (mf/g). In the cases of solutions of onium salts in polar solvents, the molarity is expressed in mol/l or in mmol/ml. Knowing the density of the solutions, it is then easy to convert into mmol/g in order to obtain elements for comparison with the Merrifield resins or PEG-type soluble polymer solutions or others. If the salt is monofunctional, the specific fonctionality (*f* expressed in mf/g) will be equal to the specific charge expressed in mmol/g. If the salt carries n times the same function, a solution containing for example one millimole of this salt per gram will have a specific functionality *f* of n.mf/g.

In the case of the onium salts tested in the preceding part of the examples (the case of the monofunctionalized onium salts), the specific charge is greater than 1 mmol.g^{-1} and can reach up to 7 mmol.g^{-1} (see Table **27** below).

Table 27

	Molecular mass	Specific charge of the support in (mmol/g)	Charge by weight of a molar solution in mg/ml
n=0; X=NTf_2	384	2.60	384
n=1; X=Cl	153.5	6.51	153.5
n=1; X=PF_6	263	3.80	263
n=1; X=BF_4	205	4.87	205
n=1; X=NTf_2	398	2.51	398
n=2; X=Cl	167.5	5.97	167.5
n=2; X=NTf_2	412	2.42	412
n=2; X=OTf	283	3.53	283
n=3; X=Cl	181.5	5.50	181.5
n=3; X=NTf_2	426	2.34	426
PEG 5000	5000	0.2	5000 (5g)

By way of comparison, the specific charge of the PEGs, which are the most commonly used soluble supports, is usually comprised between 0.1 and 1 mmol.g^{-1}.

Higher values (of the order of 10 mmol g^{-1}) are attained in the very particular case of a PEG possessing a structure of the dendrimer type such as that described by Haag (Haag et al., 2002).

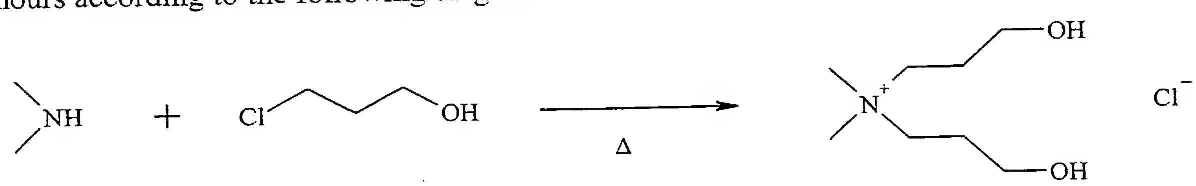
Ammonium salts having two functional arms (or more) were synthesized. The 4 substituents of the nitrogen atom can be simultaneously functionalized by multiplying the functional density of these salts by the same amount.

It is also possible to envisage synthesizing onium salts with a dendrimeric structure, whose specific charge will thus be naturally multiplied.

It must also be pointed out that the solutions of onium salts in the commonly used solvents (CH_2Cl_2, CH_3CN, DMF, H_2O...) are still not very viscous even operating at concentrations greater than 4 moles per liter. This represents a great advantage compared to the PEG solutions the concentration of which is generally less than 1 $mol.l^{-1}$

1 – Bifunctional ammonium salts:

The condensation of 3-chloropropanol and of dimethylamine is carried out at reflux in water in order to produce the bifunctionalized salt with a good yield after 24 hours according to the following diagram:

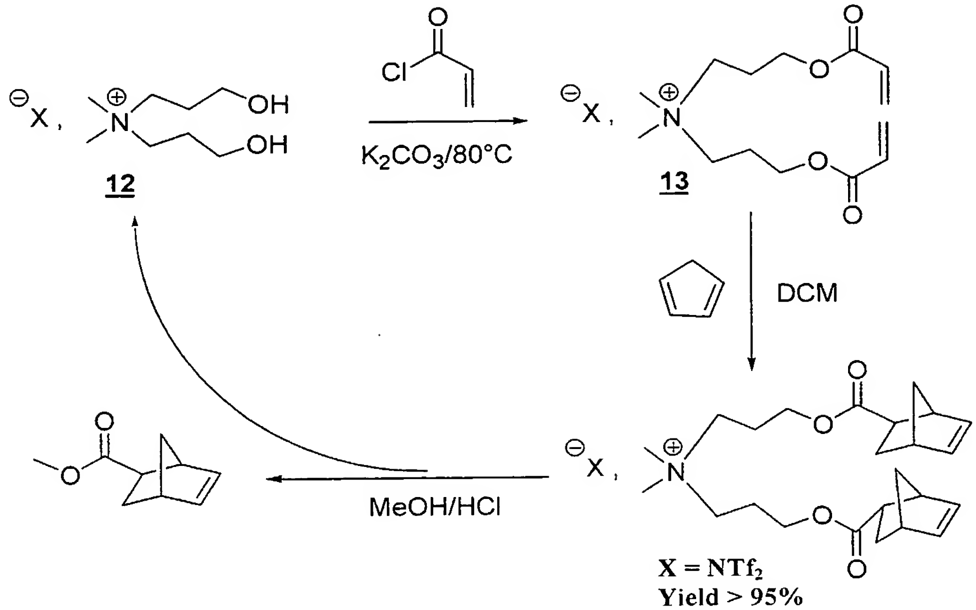


Yield = 87%

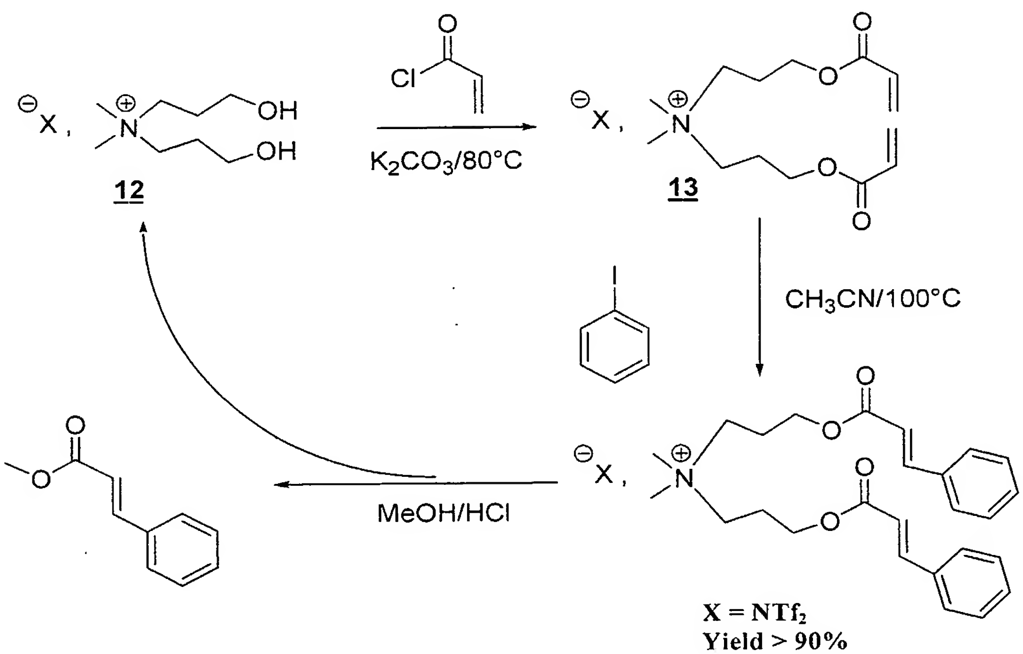
These novel supports were then tested in the same reactions as their monofunctionalized analogues. For this purpose acryloyl esters and halogenated aryls were supported and then used in Diels-Alder cycloaddition and coupling reactions.

The reaction sequences and the results obtained are presented in the diagrams below.

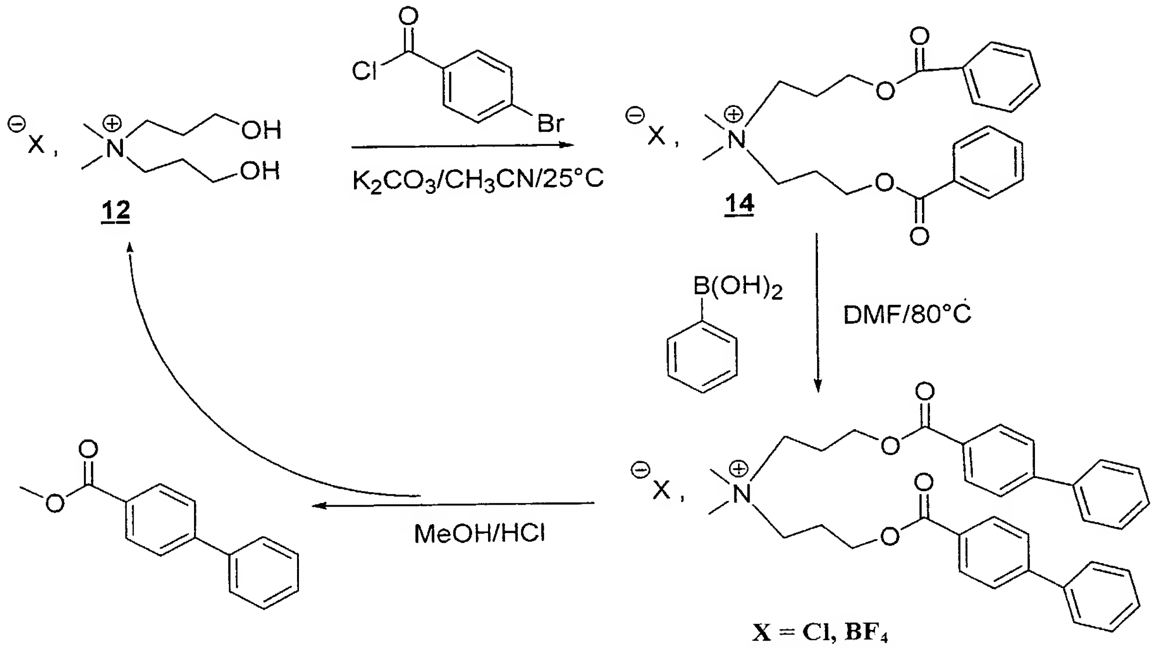
a- Cycloaddition reaction:



b- Heck coupling:



c- Suzuki coupling:



X = Cl, BF$_4$
Yield > 90%

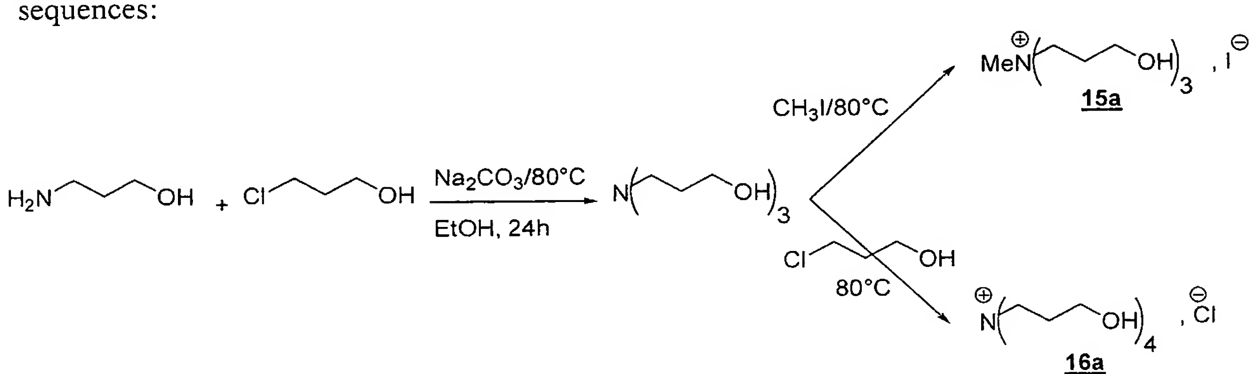
The transposition of the reactions carried out on the monofunctionalized supports to the bifunctionalized analogues causes no difference in reactivity or selectivity. Similarly, the yields of isolated products and their purity remain excellent.

The metathesis of anions was carried out either before the grafting of the substrates (the case of the bis-trifluoromethanesulphonamide anion) or after (the case of the tetrafluoroborate anion).

The chromatogram corresponding to the products of Suzuki coupling carried out on the bifunctional ammonium chloride (**14**, X=Cl) is presented in Figure 16. This chromatogram demonstrates the purity of the isolated raw product after transesterification with methanol and extraction with diethyl ether with a yield of 92%.

The monitoring of these different reactions was carried out by proton NMR as in the case of the monofunctionalized supports (see Figure 17).

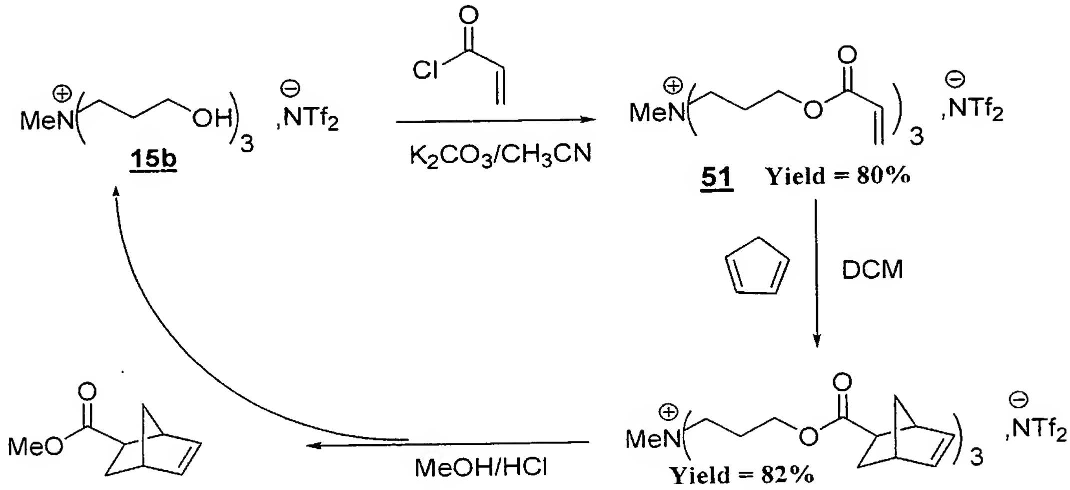
In a second stage, it was sought to further increase the functional density of the ammonium salts by tri- and tetrafunctionalization according to the following reaction sequences:

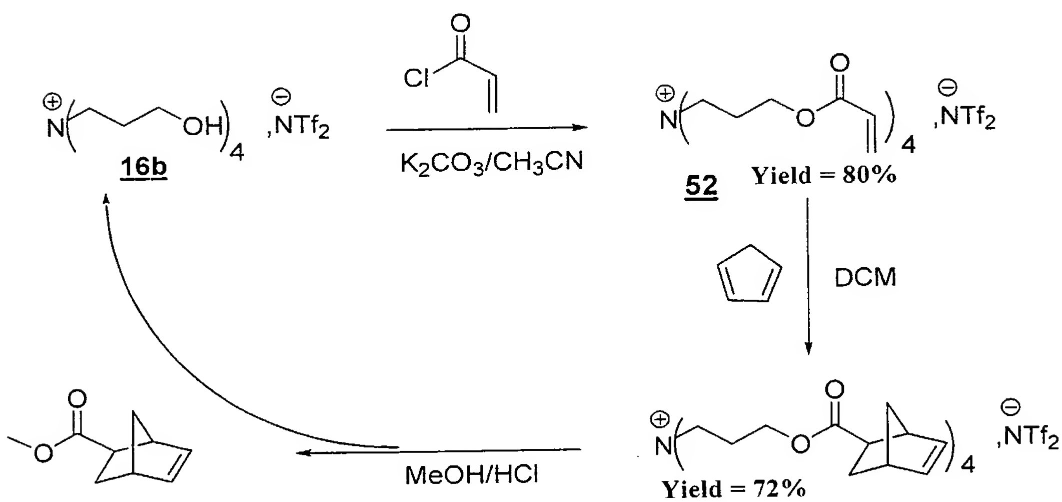


The tri- and tetra-functionalized salts were prepared from tripropanolamine by quaternization using methyl iodide or 3-chloropropanol leading to **15a** or **16a** respectively.

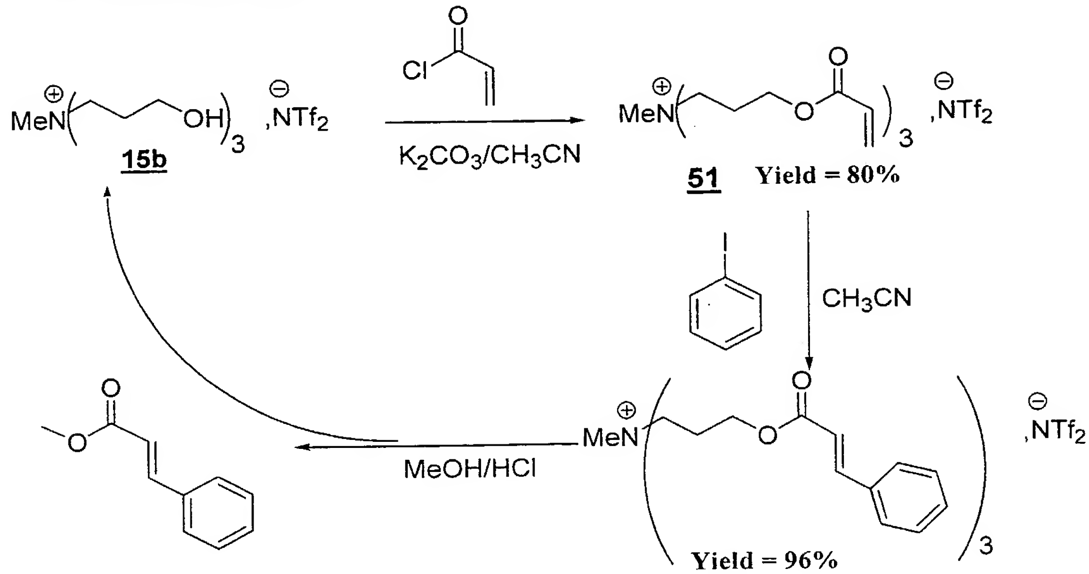
Ammonium bis-trifluoromethanesulphonamide salts derived from **15a** and **16a** obtained by metathesis in water were then used to support the acrylic ester. The latter are then used in the cycloaddition reactions as dienophiles in the presence of cyclopentadiene and in the Heck coupling reaction. The cycloaddition reaction is complete after 2 hours and allows the product to be isolated with yields greater than 75% and a purity of 97%. Similarly the Heck coupling was carried out with the same yields as those obtained with mono and bi-functionalized salts (> 95%).

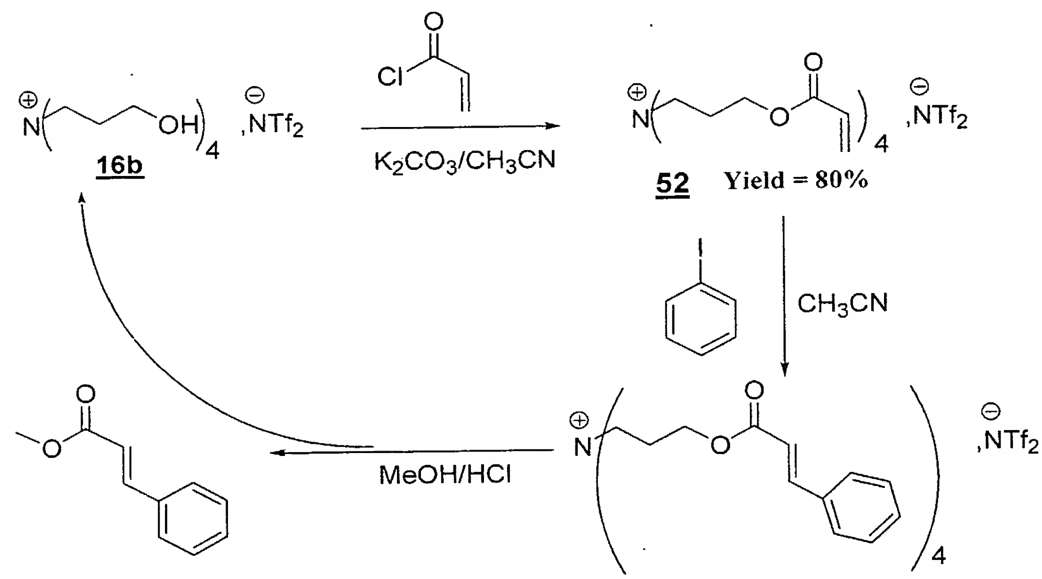
a- Cycloaddition reactions:





b- Heck couplings:

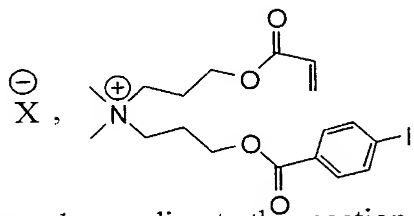




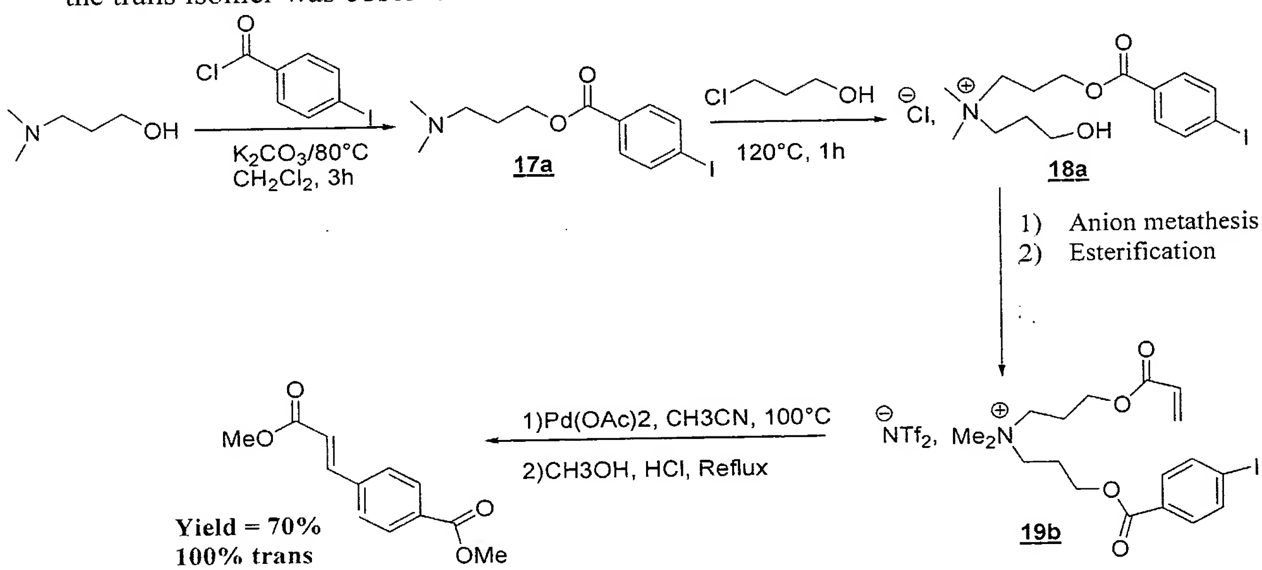
3 - Onium salts supporting the different functions:

During this study, it has been shown that onium salts have very useful potentialities and properties as soluble supports in organic synthesis. In addition to the advantages that were already explained in the first parts of this document, one of the possibilities offered by these novel soluble supports is to carry two functions (or more) of a different nature on the same cation on the condition that they do not interact with each other.

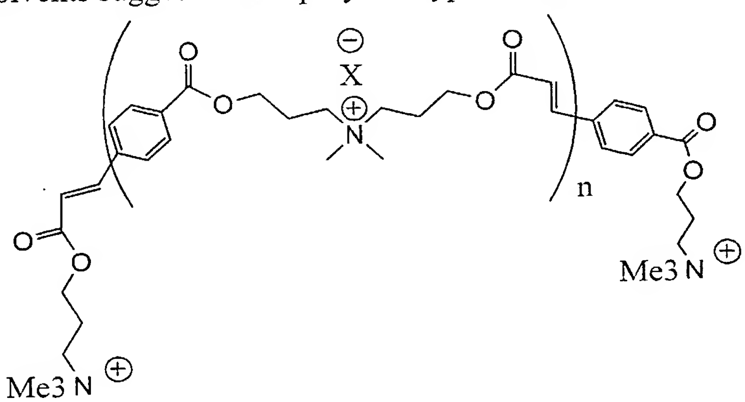
By way of illustration, we shall limit ourselves to describing ammonium salts simultaneously carrying an acrylic ester and an aryl halide of the following formula:



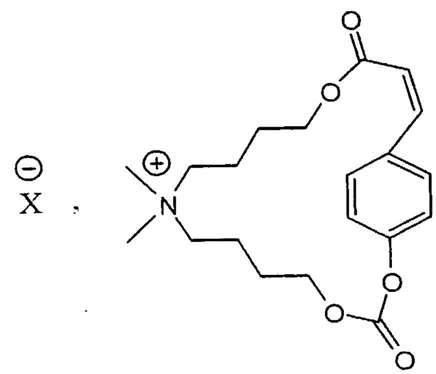
The ammonium salt prepared according to the reaction diagram below was used in the Heck coupling reaction. After one hour at 100°C in the presence of palladium acetate products were isolated, which after transesterification with methanol in the presence of a few drops of concentrated hydrochloric acid lead to the Heck coupling product with a yield of 66% and a purity greater than 98%. It is to be noted that only the trans isomer was observed in both cases.



The insolubility of the reaction product before the transesterification in the last stage in different solvents suggests that a polymer-type structure forms:



If the number of atoms is carefully chosen to lead to the cyclization product (intramolecular coupling) only the cis-form is obtained. In fact such a cyclization has been already observed under similar conditions.



The preliminary results demonstrate the importance of this family of novel supports. The potential applications can moreover also be enriched by supporting a catalyst or ligand on one of the arms, and one or more identical or different reagents on those remaining. This novel technology offers a large and unlimited choice of applications.

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